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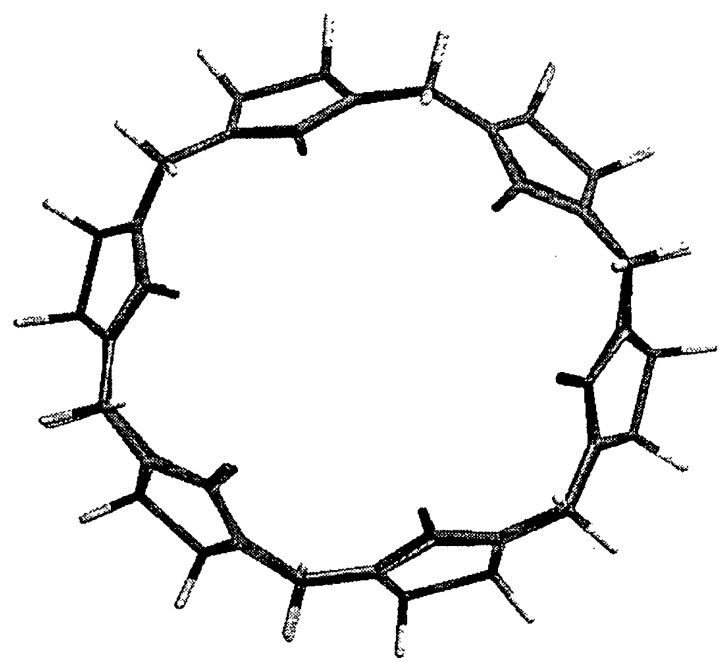
(54) Title: CUCURBITURILS AND METHOD FOR SYNTHESIS

(57) Abstract

A method for producing cucurbit[n]urils, where n is from 4 to 12, comprising mixing substituted and/or unsubstituted glycoluril with an acid and a compound that can form methylene bridges between glycoluril units, and heating the mixture to a temperature of from 20° to 120° to thereby form cucurbit[n]. Novel cucurbit[n]urils, where n = 4, 5, 7, 8, 9, 10, 11 and 12 and substituted cucurbit[s,u]urils, where s = number of substituted glycoluril units, u = number of unsubstituted units and s + u = 4 – 12 are also described.



CUCURBITURILS AND METHOD FOR SYNTHESIS

The present invention relates to a method for preparing cucurbit[n]urils and cucurbit[s,u]urils. The present invention also relates to cucurbit[n]urils, to cucurbit[s,u]urils, and to a method of separating cucurbit[n]urils and/or cucurbit[s,u]urils. The present invention also relates to novel compounds used in the preparation of cucurbit[n]urils and cucurbit[s,u]urils.

Cucurbituril is the name given to a cyclic oligomer formed by linking six (6) glycoluril units via methylene bridges. Cucurbituril was first described in the literature in 1905 in a paper by R. Behrend, E. Meyer and F. Rusche, Leibigs Ann. Chem. ; 339, 1, 1905. The macrocyclic structure of cucurbituril was first described in 1981 by W.A. Freeman et. al., "Cucurbituril", J. Am. Chem. Soc., 103 (1981), 7367-7368. Cucurbituril has a chemical formula of $C_{36}H_{36}N_{24}O_{12}$ and is a macrocyclic compound having a central cavity. An AM1 minimised structure of cucurbituril is shown in Figure 1.

The internal cavity of cucurbituril has a diameter of about 550 pm, a depth of 650 pm with portals at either end about 400 pm across. This rigid cavity has been shown to have high selectively in binding a variety of medium-small molecules and in this regard reference is made to Cintas, P., J. Inclusion Phenomena and Molecular Recognition in Chemistry; 17, 205, 1994.

The preparation of cucurbituril has generally followed the procedure first described in the article by R. Behrend et. al. published in 1905.

In German patent no. DE 196 0377, published 7 August 1997, a process for synthesising cucurbituril is described. This process includes dissolving acetylene diurea (glycoluril) in an aqueous solution of a strong mineral acid in the presence of excess formaldehyde, with warming. The water is evaporated from the mixture to completely eliminate the water from the mixture. The remaining polymer mixture is then heated to a temperature up to 145°C to complete the reaction. The applicants for this patent have stated that a yield of up to 82.4% of the theoretical yield can be obtained.

In German patent no. DE 4001139, the use of cucurbituril to remove organic compounds with hydrophobic groups, dyes, decomposition products from dyes and/or heavy metals from aqueous solutions is described. The patent actually states that a cyclic oligomer which is obtained by condensation of urea, thiourea, derivates of urea and/or derivatives of the thiourea with dialdehydes and formaldehyde is used. Although the patent states that the degree of polymerisation, n, of the cyclic oligomer varies between about 3 and about 8, the examples of the patent showing cylcic oligomers having a degree of polymerisation, n, only of 6. Example 1 shows the preparation of cucurbituril by heating glycoluril under reflux with formaldehyde.

Experiments conducted by the present inventors in following the procedure of Example 1 of DE 4001139 have shown that cucurbituril having 6 glycoluril units joined together is formed. In the words of DE 4001139, n=6 for this product. No evidence was found of any cyclic oligomer having a degree of polymerisation, n, other than 6. Indeed, a paper by Buschmann et. al., Inorgica Chimica Acta, 1992, 193, 93 states that under the synthetic conditions as described in DE 400 1139, only cucurbituril having a degree of polymerisation, n, of 6 is formed.

The present inventors have now developed a method for producing cucurbiturils having a degree of polymerisation of 4 to 12. To assist in differentiating such compounds, the present inventors have adopted the terminology "cucurbit[n]uril", where n is a number from 4 to 12, to denote the different compounds. For example, a cyclic oligomer having 4 basic glycoluril (substituted or unsubstituted) units joined together would be denoted as "cucurbit[4]uril".

In a first aspect, the present invention provides a method for producing cucurbit[n]urils, where n is from 4 to 12, comprising mixing substituted and/or unsubstituted glycoluril with an acid and a compound that can form methylene bridges between glycoluril units, and heating the mixture to a temperature of from 20°C to 120°C to thereby form cucurbit[n]urils. Preferably, n is from 5 to 10.

Preferably, the method of the present invention further comprises adding a salt to the mixture. It has been found that adding a salt to the mixture assists in achieving the synthesis of a variety of cucurbit[n]urils of differing unit sizes.

Without wishing to be bound by theory, it is believed that an ion templating effect may be occurring. Thus, selection of the particular salt can control the amount of a derived cucurbit[n]uril in the product.

It has also been found that a number of other compounds can be added to the mixture in place of the salt, or in combination with the salt, to achieve the templating effect described above. The templating effect causes the relative amount of cucurbit[n]urils of differing unit sizes to be altered if the salt or other compound is added to the mixture. For example, the salt or other compound, when added to the reaction mixture, may alter the ratio of, say, cucurbit[5]uril to cucurbit[6]uril, when that ratio is compared with the ratio of cucurbit[5]uril to cucurbit[6]uril that is produced using reaction mixtures having no salt or other compound added thereto but otherwise reacted under identical conditions.

For ease of description, such salts and other compounds will be described hereinafter throughout this specification as "templating compounds". In a preferred embodiment the method of the first aspect of the present invention further comprises adding one or more templating compounds to the mixture.

The templating compounds can be selected from a large number of compounds and indeed any compound that can alter the ratio of cucurbit[n]urils of different unit sizes produced in the method of the present invention can be used as a templating compound. The templating compound may be an organic compound, a salt of an organic compound, or an inorganic compound. Suitable compounds that may be used as a templating compound include ammonium chloride, lithium chloride, sodium chloride, potassium chloride, rubidium chloride, caesium chloride, ammonium chloride, lithium bromide, sodium bromide, potassium bromide, rubidium bromide, caesium bromide, lithium iodide, sodium iodide, potassium iodide, rubidium iodide, caesium iodide, potassium sulfate, lithium sulfate, tetrabutylammonium chloride, tetraethylammonium chloride, 0-carborane, thioacetamide, N-(1-napthyl) ethylenediamine, 2,2'-biquinoyl, p-bromoanaline, taurine, blue tetrazolium, 2-amino-3-methyl benzoic acid, indol-3-aldehyde, cystine, p-acetamidoanitine, p-aminophenol, acetamide, 4-acetamidoanitine, p-aminophenol,

acetamide, 4-aminoacetophenone, 4-dimethylaminobenzaldehyde, 2-aminobenzimadazol, bis-(4,4'-bipyridyl))-α, α'-p-xylene, red phosphorus, and lithium p-toluenesulfonate. The present inventors believe that a large number of other compounds could be suitable for use as templating compounds and therefore the above list should not be considered to be exhaustive. The anions of the acid may also be considered to be a template.

The templating compounds may be added singly to the reaction mixture or two or more templating compounds may be added to the reaction mixture.

If a salt is used as the templating compound salt that is added to the mixture is preferably a metal halide, ammonium halide, or the corresponding sulphates, or metal tosylates. It is preferred that the anion of the salt corresponds to the anion of the acid used. For example, where the acid used is hydrochloric acid, a metal chloride or ammonium chloride is the preferred salt. If sulphuric acid is used, metal sulphate or ammonium sulphate is the preferred salt. Similarly, iodide-containing salts are preferably used where hydriodic acid is the acid, and bromide-containing salts are preferably used where hydrobromic acid is used.

The acid is preferably a strong mineral acid or a strong organic acid. In principle, any acid can be used. The acid acts to catalyse the reactions taking place.

Preferred acids for use in the method of the first aspect of the present invention include sulfuric acid, hydrochloric acid, hydrobromic acid, hydroiodic acid, deuterated sulfuric acid, phosphoric acid, p-toluenesulfonic acid, and methane sulfonic acid. It will be appreciated that this list is not exhaustive and that any acid that can catalyse the reaction may be used in the method of the first aspect of the present invention.

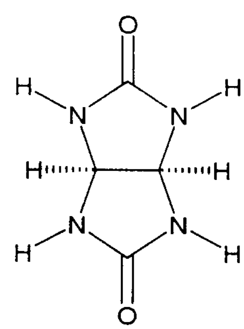
It is especially preferred that the acid has a concentration of at least 5 M.

In some embodiments of the first aspect of the present invention, a solvent may also be added to the reaction mixture. The solvent is preferably selected from trifluoroacetic acid, methanesulfonic acid and 1,1,1-trifluorethanol.

The compound that can form methylene bridges between gycoluril units is most preferably formaldehyde, paraformaldehyde, trioxane or one or more precursors for formaldehyde. For convenience, the invention will hereinafter be described with reference to the case where formaldehyde is used.

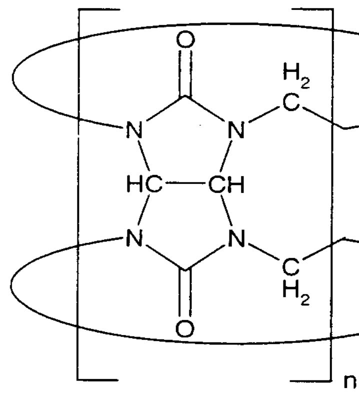
The mixture is preferably heated to temperature of from 20°C to 110°C, more preferably 60°C to 110°C, most preferably from 80°C to 110°C. It is preferred that boiling of the mixture is avoided. Heating under reflux, as required in the prior art, is not required (but may be used). Such temperature conditions are much milder than those utilised in the prior art synthesis process that led to the formation of cucurbit[6]uril. The prior art processes involved heating the mixture under reflux followed by heating to temperatures of up to 145 to 165°C. At room temperatures the present inventors have found that, cucurbit[n]uril was formed only if concentrated sulphuric acid was used as the acid. It has been found that the mixture should generally be heated to a temperature of 60°C and above to produce cucurbit[n]urils, with increased yields being obtained at temperatures on the range of 80°C to 100°C.

The glycolurils that are used in the present invention have an unsubstituted structure as shown in formula 1 below:



(Formula 1)

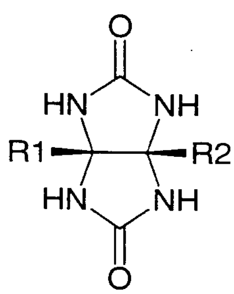
The general structure for the cucurbit[n]urils synthesised in accordance with the process of the present invention is shown in formula 2 below:



wherein n = 4 to 12, preferably 4 to 10.

(Formula 2)

Substituted and unsubstituted glycolurils, or a mixture thereof, may be used to synthesise cucurbit[n]uril in accordance with the present invention. Substituted glycolurils have the general formula as shown in formula 3 below:



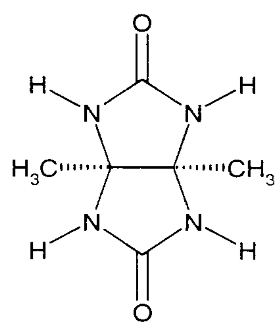
(Formula 3)

wherein R_1 and R_2 are the same or different and selected from an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical or R_1 and R_2 form a cyclic hydrocarbon radical. The hydrocarbon radical for substituents R_1 and R_2 may include alkyl, alkenyl, alkynyl, aryl and heterocyclyl radicals. There are large numbers of substituted glycolurils known in the literature. Particular reference is made to a review article by Harro Petersen in Synthesis, 1973, 243-293, which contains a list of about 30 substituted glycolurils. The entire contents of this review article are hereby expressly incorporated into this specification by cross reference. The literature since the

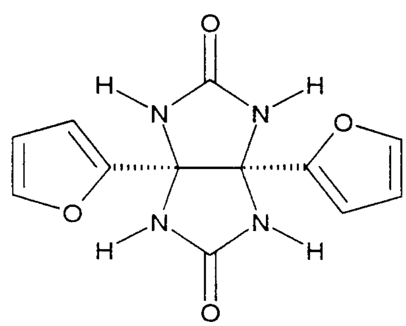
Petersen article has disclosed several other examples of substituted glycolurils and it is believed that essentially any α,β-diketone could be used to make a glycoluril.

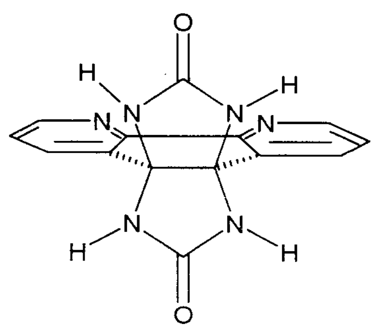
Investigations conducted by present inventors have shown that cucurbit[n]uril-like systems can be synthesised with many of the substituted glycolurils, preferably when used in conjunction with unsubstituted glycolurils. The following substituted glycoluril compounds have been prepared and used to synthesise substituted cucurbit[n]urils:

(Formula 4)

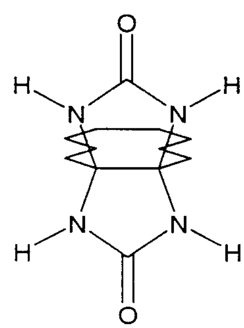


(Formula 5)





(Formula 6)



(Formula 7)

The compounds of formulae 5, 6 and 7 above are novel and accordingly, in another aspect, the present invention provides a substituted glycoluril compound of formula 5, formula 6 or formula 7.

The synthesis of substituted cucurbit[n]urils opens the possibility of being able to chemically link the substituted cucurbit[n]uril to a substrate or to chemisorb them onto a substrate. The solubility characteristics of the product may also be manipulated by selection of appropriate substituents.

As mentioned earlier, cucurbit[6]uril was first characterised and synthesised in 1905. However, the present inventors believe that cucurbit[n]uril, where n=4, 5, 7, 8, 9, 10, 11 or 12 has never previously been synthesised. Accordingly, in a further aspect, the present invention provides cucurbit[n]uril, where n = 4, 5, 7, 8, 9, 10, 11 or 12. Preferably, n = 5, 7, 8, 9 or 10.

The present also provides substituted cucurbit[n]urils, where n = 4, 5, 6, 7, 8, 9, 10, 11 or 12. In order to clarify nomenclature when substituted cucurbiturils are formed, the present inventors have proposed that substituted cucurbiturils in accordance with the present invention be identified by the scheme "cucurbit[s,u]uril", where s = the number of substituted glycoluril units and u = the number of unsubstituted glycoluril units in the cucurbituril. Using this nomenclature, the present invention also provides cucurbit[s,u]uril, where s and u are as defined above and s+u=4 to 12, preferably 5 to 10.

In all of the experimental work conducted by the present inventors to date in relation to substituted cucurbiturils,, the substituted cucurbiturils have incorporated both substituted and unsubstituted glycoluril units into the cucurbituril structure. Thus, it is preferred that u does not equal zero. If s equals zero, cucurbit[s,u]uril is equivalent to cucurbit[n]urils.

The substituted cucurbit[n]urils are preferably synthesized from substituted glycoluril or a mixture of substituted and unsubstituted glycoluril. The substituents may be as described above.

In order to show the structure of cucurbit[n]uril in cases where n = 4, 5, 7 or 8, minimised chemical structures were prepared using PC-Spartan, a molecular modelling and visualisation package. The minimised structures are shown as formulae 8 to 11 in Figures 2 to 5:

The minimised structures of Formulae 8 to 11 clearly show the inner cavity of the cucurbituril. As the value of n increases, the size of the inner cavity increases, which enables different compounds to fit into the inner cavity.

The reaction product of the process of the present invention contains a mixture of different cucurbit[n]urils or cucurbit[s,u]urils. There are several methods that could be used to separate and purify these products and these are described below:

Successive Recrystallisation

All of the cucurbit[n]urils that have been observed are apparently soluble in acid solutions. Cucurbit[5 or 7 or 8 or 10]uril have been purified by successive recrystallisations from acid solutions. Because of the similar nature of the cucurbiturils, this is a slow process with more than 10 recrystallisations required to purify cucurbit[7]uril. As shown in the German patents cucurbit[6]uril can be obtained in a relatively pure state from a single recystallisation process.

Selective dissolution/precipitation

We have been able to demonstrate that different cucurbiturils have markedly different solubilities in various salt solutions. It is possible to separate cucurbit[6]uril and cucurbit[7]uril from a mixture containing cucurbit[5-8]urils by dissolving cucurbit[6 or 7]uril out of the complex mixture using a 0.1M $Na_2 SO_4$ solution.

We have also demonstrated the use of selective precipitation as a purification method. A solution of cucurbit[6]uril and cucurbit[7]uril was mixed with bis(4,4'-dipyridyl)-α,α'-p-xylene. ^{1}H NMR showed a decrease in signal due to the cucurbit[7]uril and bis(4,4'-dipyridyl)-α,α'-p-xylene with several crystals depositing out of the sample.

According to another aspect, the present invention comprises separating a mixture of cucurbit[n]urils, where n = 4 to 12, by mixing the mixture of cucurbit[n]urils with a salt solution in which at least one of the cucurbit[n]urils, but not all of the cucurbit[n]urils, dissolves, separating solids in which at least one of the cucurbit[n]urils, but not all of the cucurbit[n]urils, dissolves, separating solids from the solution recovering the dissolved at least one cucurbit[n]urils from the solution. This method may also be used to separate mixtures of different substituted cucurbit[s,u]urils.

As an example, lithium chloride in hydrochloric acid solutions selectively assists the crystallisation of cucurbit[6]uril and cucurbit[8]uril leaving cucurbit[5]uril and cucurbit[7]uril in solution.

Potassium chloride in hydrochloric acid solutions selectively assists the crystallisation of cucurbit[5]uril and cucurbit[8]uril leaving cucurbit[6]uril and cucurbit[7]uril in solution.

Any of the salt complexed cucurbit[n]urils can be separated from their salt by a process of desalting on ion exchange resins such as Dowex 50. Dissolved in formic acid water, the mixtures are loaded onto the resin and the salts eluted with dilute hydrochloric acid/formic acid solutions until satisfactory salt removal and then the final recovery of the cucurbit[n]uril is achieved by elution with 5M or higher of aqueous hydrochloric acid.

Chromatographic Separation

Both Thin Layer Chromatography (TLC) and High Pressure Liquid Chromatography (HPLC) have demonstrated ability to separate out various oligomers of cucurbit[n]uril. Both of these systems are under continuing investigation. TLC using a silica stationary phase and 0.1M Hydrochloric acid as the mobile phase resulted in a mixture of cucurbit[n]urils separating into several bands. HPLC separation has been attempted using a C-18 stationary phase and 0.5M Na_2SO_4 mobile phase. The retention times of recrystallised samples of cucurbit[6]uril and cucurbit[7]uril were comparable with peaks found in mixed samples of crude cucurbit[n]urils.

In a further aspect, the present invention provides a method for separating a mixture of cucurbit[n]urils, where n = 4 to 10, by dissolving the mixture of cucurbit[n]urils and subjecting the thus-formed solution of cucurbit[n]urils to chromatographic separation. This method may also be used to separate mixtures of cucurbit[s,u]urils.

In addition, polymer resins as chromatographic supports, such as, Dowex or Sephadex ion exchange columns or polyamines are effective in the purification of cucurbit[n]urils. The eluant most commonly used was 30-50% aqueous formic acid or a mixture of formic acid 98% and aqueous hydrochloric acid 0.5M in a ratio of 1:2 respectively. Samples sizes of 1 to 2 gm were able to be purified on a bed of 25cm of resin.

In order to more fully understand the present invention, the proposed reaction mechanism will be discussed hereunder. It is to be understood that the following reaction mechanism is a proposed mechanism and the present invention should not be considered to be limited thereto. The proposed reaction mechanism hereunder should be read in conjunction with Figures 1a, 1b, 1c and 1d.

The synthesis of cucurbit[n]uril or substituted cucurbit[n]uril (where n equals the number of glycouril units marking up cucurbituril) is an acid catalysed process. In the mechanism detailed below the first important intermediate **1** has been isolated and is the

reaction of a glycoluril with four equivalents of formaldehyde. The dehydration of this tetrol to the cyclic diether **2** has been demonstrated by the isolation of pure **2** where R = phenyl. The intermediates **A** or **B** are both produced through a series of acid catalysed steps. This mechanism is not prescriptive, as it is possible for either **A** or **B** to be produced without going through **1** or **2**. Similarly, it is possible for glycoluril units to begin linking on one side prior to reaction with formaldehyde on the other. This is a dynamic process with multiple reversible reaction steps. The mechanism shown here is only to be considered representative of the many possibilities.

The reaction from glycoluril to cucurbit[n]uril involves a number of intermediates produced through reversible reaction steps. The influences acting on the balance of these reversible steps are many and some can be manipulated at a variety of points there by effecting the out come of the reaction.

Examples

The following examples illustrate preferred embodiments of the present invention:

Example 1

Synthesis of cucurbit[n]urils

1.5 g – glycoluril

6.9 ml – mineral acid (hydrochloric 36%, hydrobromic 48%, hydriodic 47% or sulphuric acid 98% or 50%) or organic acid (para toluene sulphonic acid)

1.5 ml – aqueous formaldehyde 30%

5 mmol – of the corresponding alkali metal halide, ammonium halide or the corresponding sulphates in the case of sulphuric acid or alkali metal tosylates

600 mg – red phosphorus (*this was added to reaction mixtures when hydriodic acid was used*).

The glycoluril (1.5gm, 10.6mmol) was dissolved or suspended in the appropriate acid (6.9ml). Then in the cases where a salt was used to manipulate reaction products the alkali metal ion or ammonium salt (5mmol) with the corresponding anion appropriate to the acid was added. To this mixture at room temperature was added formaldehyde (1.5ml) and within 5-10min, the mixture set as a gel (note 1). After standing 3 hrs (note 2), heat was applied raising the temperature to 100°C (note 3) whereby the gel liquefied. Heating

and stirring was maintained for 2-3 hr (note 4). The reaction mixtures were cooled and in the case of HC1 and HBr all volatiles were removed *in vacuo* at temperatures no higher than 50°C. The residues were dissolved in the appropriate acid and evaporated again, this was repeated twice (note 5).

For remaining acids, the products were isolated by adding methanol (10ml) and collecting the resultant precipitate by filtration. The solid material was washed with methanol and acetone and air dried. The red phosphorus was removed by filtration before the addition of methanol.

Products have been isolated by a process of recyrstallisation using hydrochloric acid or hydrobromic acid at varying concentrations to effect crystallisation. The total yield was >90% except in the case of hydriodic acid where yields were 30-80% depending on the salt used. In all cases the range of isomers was produced *ie* cucurbit[n]urils with n= 4, 5, 6, 7, 8, 9, etc. The maximum production of each of these was achieved as follows:-

n = 4, <=1% in varying amounts under all conditions,

n = 5, 55-75%, with NaI, KI, or RbI in hydriodic acid,

n = 6, 80%, with CsCl in hydrochloric acid,

n = 7, 52-65%, with no salts or with LiI in hydriodic acid,

n = 8, 7-9%, with LiBr, or RbBr in hydrobromic acid, or LiOTs in aqueous pTsOH,

n = 9, <=5%, with NH_4Cl in hydrochloric acid,

n>=10, <=2%, in varying amounts under all conditions.

Notes A

1. Following the addition of formaldehyde there is an exothermic reaction. On larger scale the reaction mixture is cooled in an ice bath. Formaldehyde can be substituted by paraformaldehyde or trioxane or any formaldehyde producing precursor.

2. Proceeding to the next stage of the reaction procedure after 1hr or 1 month at room temperature makes little difference to the out come except in the case of concentrated sulphuric acid where the reaction continues to cucurbit[n]urils at room temperature.

3. A reaction temperature of 60°C and above is sufficient to give cucurbit[n]urils but at the lower temperatures with extended reaction times to achieve completion, up to 60hrs. The given yields above for the larger unit cucurbit[>=7]uril are on average increased a further 50% on the tabled yields.

4. In some cases pressure was generated during heating. In the event of a pressure build up the pressure was released

5. The repeated dissolving and evaporation was primarily carried out to remove excess formaldehyde and volatile formaldehyde by products.

<u>Example 2</u>

Synthesis Cucurbit[s,u]urils

The same templating controls are applied to substituted cucurbit[n]urils either by the above method where glycoluril used is substituted or as described below.

A mixture of tetracyclic ether B (2.5 mmol) and glycoluril (0.355 gm, 2.5 mmol) was dissolved or suspended in the appropriate acid (6.9ml) (note 1). Then in the cases where a salt was used to manipulate reaction products the alkali metal ion or ammonium salt (5mmol) with the corresponding anion appropriate to the acid was added. Heat was then applied to the reaction mixture, which was maintained at a temperature of 100°C for 3hrs (Note 2). The reaction mixture was cooled to room temperature and the products were isolated by adding methanol (10ml) and collecting the resultant precipitate by filtration. The solid material was washed with methanol and acetone and air dried. Further purification was effected by recrystalisation from aqueous hydrochloric acid or hydrobromic acid or dissolving in formic acid and precipitating by the addition of water.

The composition of these mixed substituted cucurbit[n]urils was determined by Electrospray Mass Spectroscopy.

Notes B

1. The Tetracyclic ether B refers to B, described in the mechanistic scheme where the substituents R are alkyl, aryl, phenanthroline and pyridyl.

2. Para toluene sulphonic acid was the acid of choice for the tetracyclic ethers where R equals aryl or pyridyl and the temperature of the reaction mixture was maintained at 110°C.

3.

Example 3

Analysis of Cucurbituril Mixture

The analysis of the cucurbituril reaction mixture is routinely carried out by ^{13}C NMR. The present inventors have been able to achieve the x-ray crystal structure for cucurbit[5]uril, cucurbit[8]uril and cucurbit[10]uril. These are shown in Figure 5a, in which Formula 12 is cucurbit[5]uril, Formula 13 is cucurbit[8]uril and Formula 14 is cucurbit[10]uril. Waters, salts etc of crystallisation are not shown.

(Cucurbit[6]uril is well established in the literature.) Solutions of pure cucurbit[7]uril, as determined by ^{13}C NMR have been prepared and Electro-Spray Mass Spectroscopy has confirmed the presence of only cucurbit[7]uril. *(While pure cucurbit[7]uril is a crystalline material it is difficult to grow crystals of X-ray quality.)* From these pure compounds the inventors have observed a trend in the ^{13}C NMR chemical shift of both the methylene and methine carbons of the cucurbit[n]uril. This trend has allowed us to identify cucurbit[9]uril, cucurbit[11]uril and cucurbit[12]uril in the reaction mixture. The table below shows the observed ^{13}C cehmical shifts for the unambiguously identified cucurbit[5]uril, cucurbit[6]uril, cucurbit[7]uril, cucurbit[8]uril and cucurbit[10]uril. The predicted and observed values for cucurbit[9]uril, cucurbit[11]uril, cucurbit[12]uril and cucurbit[13]uril are also provided.

Curcurbit[n]uril n=	Methine C Observed* (ppm)	Methine C Calc'd (ppm)	Methylene C Observed* (ppm)	Methylene C Calc'd (ppm)
4	-	68.54	-	48.75
5	69.84	69.87	50.58	50.68
6	70.98	70.96	52.29	52.17
7	71.90	71.88	53.48	53.43
8	72.70	72.68	54.49	54.53
9		73.38		55.49
10	73.98	74.01	56.32	56.35
11		74.58		57.13
12		75.10		57.84
13		75.58		58.50

* These values were recorded on pure isolated materials.

The results of this Table are graphically shown in Figures 6 and 7.

Using this information the inventors have now identified cucurbit[9]uril (methine carbon 73.45 ppm and methylene carbon 55.42 ppm) in standard reaction mixtures. Cucurbit[11]uril and cucurbit[12]uril have only been observed by the methylene carbon when ^{13}C labelled formaldehyde was used as a reactant. Under these conditions the cucurbit[11]uril methylene carbon was observed at 56.86 ppm and the cucurbit[12]uril methylene carbon was observed at 57.75 ppm.

The inventors have routinely used the integration of ^{13}C NMR over the methine region of the spectra to determine the relative amounts of each cucurbit[n]uril in the mixture. In doing so it was assumed that the signal response for each species is related to the number of methine carbons for that cucurbit[n]uril and that there is little difference in signal response between the different cucurbit[n]urils. The integration-percent is then directly proportional to the mass percent of each component.

Example 4

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (250 mg) and hydrochloric acid (36 % w/v,2000 mL) were placed in a reaction flask. Formalin (40% w/v) (250 μL) was added in one portion and the reaction mixture heated to 100°C for 15 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator.

Yield ~30 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	58%
cucurbit[6]uril	42%
cucurbit[7]uril	%
cucurbit[8]uril	%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 5

Synthesis of cucurbit[n]urils in sulfuric acid.

Glycoluril (500 mg) and sulfuric acid (9 M, 500 mL) were placed in a reaction flask. Formalin (40% w/v) (250 μL) was added in one portion and the reaction mixture heated to 100°C for 15 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and

Yield ~85 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	21%
cucurbit[6]uril	64%
cucurbit[7]uril	14%
cucurbit[8]uril	1%
cucurbit[9]uril	<1%

cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 6

Synthesis of cucurbit[n]urils in sulfuric acid.

Glycoluril (1.5 g) and sulfuric acid (9 M, 6.9 mL) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	26%
cucurbit[6]uril	49%
cucurbit[7]uril	19%
cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 7

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (77 mg) and hydrochloris acid (10 M, 0.4 mL) were placed in a reaction flask. Paraformaldehyde (33 mg) was added in one portion and the reaction mixture heated to 105°C for 2.5 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	19%
cucurbit[6]uril	54%
cucurbit[7]uril	21%

cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 8

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (77 mg) and hydrochloric acid (9 M, 0.4 mL) were placed in a reaction flask. Paraformaldehyde (33 mg) was added in one portion and the reaction mixture heated to 105°C for 2.5 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	18%
cucurbit[6]uril	56%
cucurbit[7]uril	19%
cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 9

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (77 mg) and hydrochloric acid (8 M, 0.4 mL) were placed in a reaction flask. Paraformaldehyde (33 mg) was added in one portion and the reaction mixture heated to 105°C for 2.5 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	15%
cucurbit[6]uril	58%
cucurbit[7]uril	23%
cucurbit[8]uril	4%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 10

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (77 mg) and hydrochloric acid (7 M, 0.4 mL) were placed in a reaction flask. Paraformaldehyde (33 mg) was added in one portion and the reaction mixture heated to 105°C for 2.5 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	18%
cucurbit[6]uril	57%
cucurbit[7]uril	23%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 11

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (77 mg) and hydrochloric acid (5 M, 0.4 mL) were placed in a reaction flask. Paraformaldehyde (33 mg) was added in one portion and the reaction mixture heated to 105°C for 2.5 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	10%
cucurbit[6]uril	60%
cucurbit[7]uril	27%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 12

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (2.4 g) and hydrochloric acid (36 % w/v, 2 mL) were placed in a reaction flask. Formalin (40% w/v) (2.4 mL) was added in one portion and the reaction mixture heated to 110°C for 3 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	6%
cucurbit[6]uril	60%
cucurbit[7]uril	30%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 13

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (2.4 g) and hydrochloric acid (36 % w/v, 2 mL) were placed in a reaction flask. Formalin (40% w/v) (2.4 mL) was added in one portion and the reaction mixture heated to 110°C for 18 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	6%
cucurbit[6]uril	60%
cucurbit[7]uril	30%
cucurbit[8]uril	2%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 14

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (2.1 g) and hydrochloric acid (36 % w/v, 3 mL) were placed in a reaction flask. Paraformaldehyde (887 mg) was added in one portion and the reaction mixture heated to 110°C for 18 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	9%
cucurbit[6]uril	52%
cucurbit[7]uril	29%
cucurbit[8]uril	8%
cucurbit[9]uril	<1%

cucurbit[10]uril <1%

cucurbit[11]uril <1%

Example 15

Synthesis of cucurbit[n]urils in hydrobromic acid.

Glycoluril (2.1 g) and hydrobromic acid (48 % w/v, 3 mL) were placed in a reaction flask. Paraformaldehyde (887 mg) was added in one portion and the reaction mixture heated to 100°C for 18 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	8%
cucurbit[6]uril	50%
cucurbit[7]uril	29%
cucurbit[8]uril	12%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 16

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (105 mg) and hydrochloric acid (36 % w/v, 0.4 mL) were placed in a reaction flask. Formalin (40% w/v) (105 μL) was added in one portion and the reaction mixture heated to 60°C for 65 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	4%
cucurbit[6]uril	64%

cucurbit[7]uril	23%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 17

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (77 mg) and hydrochloric acid (8 M, 0.4 mL) were placed in a reaction flask. Paraformaldehyde (33 mg) was added in one portion and the reaction mixture heated to 105°C for 2.5 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	13%
cucurbit[6]uril	60%
cucurbit[7]uril	23%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 18

Synthesis of cucurbit[n]urils in phosphoric acid.

Glycoluril (1.5 g) and phosphoric acid (conc, 6.9 mL) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 18 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	10%
cucurbit[6]uril	60%
cucurbit[7]uril	28%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 19

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (1.02 g) and hydrochloric acid (36 % w/v, 0.6 mL) were placed in a reaction flask. Paraformaldehyde (430 mg) was added in one portion and the reaction mixture heated to 100°C for 15 hours. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	4%
cucurbit[6]uril	53%
cucurbit[7]uril	27%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 20

Synthesis of cucurbit[n]urils in deuterated sulfuric acid.

Glycoluril (78 mg) and deuterated sulfuric acid (conc, 0.4 mL) were placed in a reaction flask. Formalin (40% w/v) (73 μL) was added in one portion and the reaction mixture

heated to rt°C for 2 months. The reaction mixture was cooled and the products were analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	>95%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 21

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (108 mg) and hydrochloric acid (36 % w/v, 0.4 mL) were placed in a reaction flask. Formalin (40% w/v) (108 μL) was added in one portion kept at room temperature for 1 month. The products were analysed by ^{13}C NMR.

Yield -No cucurbiturils present NMR suggests oligomeric product.

Example 22

Synthesis of cucurbit[n]urils in hydrochloric acid.

Glycoluril (1000 g) and hydrochloric acid (36 % w/v, 1420 mL) were placed in a reaction flask. Paraformaldehyde (422 g) was added in one portion and the reaction mixture heated to 105°C for 18 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator.

Yield quantitative mass recovery and >98 % cucurbit[n]urils by NMR
Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	19%

cucurbit[6]uril	47%
cucurbit[7]uril	27%
cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 23

Synthesis of cucurbit[n]urils in p-toluenesulfonic acid.

Glycoluril (1 g) and p-toluenesulfonic acid (~90 % w/w, 6.9 g) were placed in a reaction flask. Formalin (40% w/v) (1 mL mg) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	6%
cucurbit[6]uril	68%
cucurbit[7]uril	20%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 24

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (146.5 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (65.5 mg) was added in one portion and the reaction mixture heated to 90°C for 22 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	6%
cucurbit[6]uril	52%
cucurbit[7]uril	33%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 25

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (197.6 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (91.1 mg) was added in one portion and the reaction mixture heated to 90°C for 23.5 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	8%
cucurbit[6]uril	54%
cucurbit[7]uril	30%
cucurbit[8]uril	8%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 26

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (302.6 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (130.3 mg) was added in one portion and the reaction mixture

heated to 90°C for 23.5 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	54%
cucurbit[7]uril	32%
cucurbit[8]uril	11%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 27

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (497.3 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (204.0 mg) was added in one portion and the reaction mixture heated to 90°C for 25 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	0%
cucurbit[6]uril	77%
cucurbit[7]uril	23%
cucurbit[8]uril	0%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 28

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (144.6 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (61.3 mg) was added in one portion and the reaction mixture heated to 70°C for 22.5 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	0%
cucurbit[6]uril	49%
cucurbit[7]uril	34%
cucurbit[8]uril	17%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 29

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (145.2 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (62.9 mg) was added in one portion and the reaction mixture heated to 80°C for 24 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	4%
cucurbit[6]uril	56%
cucurbit[7]uril	28%
cucurbit[8]uril	11%

cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 30

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (142.5 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (60.7 mg) was added in one portion and the reaction mixture heated to 100°C for 25 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	59%
cucurbit[7]uril	32%
cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 31

Synthesis of cucurbit[n]urils in methane sulfonic acid.

Glycoluril (148.3 mg) and methane sulfonic acid (neat, 1.5 mL) were placed in a reaction flask. Paraformaldehyde (60.2 mg) was added in one portion and the reaction mixture heated to 110°C for 27 hours. The reaction mixture was cooled and the collected using a centrifuge.The collected solid was then dried at 80°C overnight.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (% of recovered product)

cucurbit[5]uril	0%

cucurbit[6]uril	93%
cucurbit[7]uril	7%
cucurbit[8]uril	0%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 32

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (146.9 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (~18 mg) were placed in a reaction flask. Paraformaldehyde (64.2 mg) was added in one portion and the reaction mixture heated to 90°C for 22.5 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	52%
cucurbit[7]uril	33%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 33

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (200.5 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (102.7 mg) were placed in a reaction flask. Paraformaldehyde (94.2 mg) was added in one portion and

the reaction mixture heated to 90°C for 24 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	8%
cucurbit[6]uril	53%
cucurbit[7]uril	29%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

<u>Example 34</u>

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (299.0 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (152.4 mg) were placed in a reaction flask. Paraformaldehyde (126.2 mg) was added in one portion and the reaction mixture heated to 90°C for 24 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	57%
cucurbit[7]uril	33%
cucurbit[8]uril	7%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 35

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (501.9 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (166.2 mg) were placed in a reaction flask. Paraformaldehyde (207.9 mg) was added in one portion and the reaction mixture heated to 90°C for 25 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	0%
cucurbit[6]uril	63%
cucurbit[7]uril	28%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 36

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (145.0 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (53.4 mg) were placed in a reaction flask. Paraformaldehyde (62.5 mg) was added in one portion and the reaction mixture heated to 70°C for 22.5 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	0%
cucurbit[6]uril	48%
cucurbit[7]uril	32%
cucurbit[8]uril	20%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 37

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (146.9 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (53.4 mg) were placed in a reaction flask. Paraformaldehyde (64.0 mg) was added in one portion and the reaction mixture heated to 80°C for 24 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	4%
cucurbit[6]uril	48%
cucurbit[7]uril	29%
cucurbit[8]uril	19%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 38

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (142.7 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (48.6 mg) were placed in a reaction flask. Paraformaldehyde (60.7 mg) was added in one portion and the reaction mixture heated to 100°C for 25 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	2%
cucurbit[6]uril	53%
cucurbit[7]uril	31%
cucurbit[8]uril	14%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 39

Synthesis of cucurbit[n]urils in methane sulfonic acid using o-carborane as an added template.

Glycoluril (145.5 mg), methane sulfonic acid (neat, 1.5 mL) and o-carborane (49.9 mg) were placed in a reaction flask. Paraformaldehyde (60.7 mg) was added in one portion and the reaction mixture heated to 110°C for 27 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	0%

cucurbit[6]uril	65%
cucurbit[7]uril	26%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 40

Synthesis of cucurbit[n]urils in hydrochloric acid using thioacetamide as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and thioacetamide (12.8 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	0%
cucurbit[6]uril	64%
cucurbit[7]uril	36%
cucurbit[8]uril	0%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 41

Synthesis of cucurbit[n]urils in hydrochloric acid using N-(1-napthyl)ethylenediamine as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and N-(1-napthyl)ethylenediamine (44.1 mg) were placed in a reaction flask. Paraformaldehyde

(60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	12%
cucurbit[6]uril	53%
cucurbit[7]uril	23%
cucurbit[8]uril	12%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 42

Synthesis of cucurbit[n]urils in hydrochloric acid using 2,2'-biquinoyl as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and 2,2'-biquinoyl (43.6 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	6%
cucurbit[6]uril	62%
cucurbit[7]uril	26%
cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 43

Synthesis of cucurbit[n]urils in hydrochloric acid using p-bromoaniline as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and p-bromoaniline (29.3 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	11%
cucurbit[6]uril	36%
cucurbit[7]uril	36%
cucurbit[8]uril	15%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 44

Synthesis of cucurbit[n]urils in hydrochloric acid using tetrabutylammonium chloride as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and tetrabutylammonium chloride (47.3 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	55%
cucurbit[7]uril	25%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 45

Synthesis of cucurbit[n]urils in hydrochloric acid using taurine as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and taurine (21.3 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	16%
cucurbit[6]uril	51%
cucurbit[7]uril	23%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 46

Synthesis of cucurbit[n]urils in hydrochloric acid using blue tetrazolium as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and blue tetrazolium (123.7 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion

and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	7%
cucurbit[6]uril	55%
cucurbit[7]uril	23%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 47

Synthesis of cucurbit[n]urils in hydrochloric acid using 2-amino-3-methyl benzoic acid as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and 2-amino-3-methyl benzoic acid (25.7 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	55%
cucurbit[7]uril	25%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 48

Synthesis of cucurbit[n]urils in hydrochloric acid using indol-3-aldehyde as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and indol-3-aldehyde (24.7 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	70%
cucurbit[7]uril	25%
cucurbit[8]uril	2%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 49

Synthesis of cucurbit[n]urils in hydrochloric acid using cystine as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and cystine (40.9 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%

cucurbit[6]uril	55%
cucurbit[7]uril	25%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 50

Synthesis of cucurbit[n]urils in hydrochloric acid using p-acetamidoaniline as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and p-acetamidoaniline (25.5 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	55%
cucurbit[7]uril	25%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 51

Synthesis of cucurbit[n]urils in hydrochloric acid using p-aminophenol as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and p-aminophenol (18.6 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion

and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	13%
cucurbit[6]uril	39%
cucurbit[7]uril	36%
cucurbit[8]uril	12%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

<u>Example 52</u>

Synthesis of cucurbit[n]urils in hydrochloric acid using acetamide as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and acetamide (10.0 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	9%
cucurbit[6]uril	31%
cucurbit[7]uril	39%
cucurbit[8]uril	17%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Exmaple 53

Synthesis of cucurbit[n]urils in hydrochloric acid using 4-aminoacetophenone as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and 4-aminoacetophenone (23.0 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	9%
cucurbit[6]uril	44.5%
cucurbit[7]uril	35%
cucurbit[8]uril	12%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 54

Synthesis of cucurbit[n]urils in hydrochloric acid using 4-dimethylaminobenzaldehyde as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and 4-dimethylaminobenzaldehyde (25.4 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	55%
cucurbit[7]uril	25%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 55

Synthesis of cucurbit[n]urils in hydrochloric acid using 2-aminobenzimadazol as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and 2-aminobenzimadazol (22.6 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 2 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	9%
cucurbit[6]uril	40%
cucurbit[7]uril	30%
cucurbit[8]uril	11%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 56

Synthesis of cucurbit[n]urils in hydrochloric acid using bis-(4,4'-bipyridyl)-α, α'-p-xylene as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and bis-(4,4'-bipyridyl)-α, α'-p-xylene (110.8 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 2 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	8%
cucurbit[6]uril	42%
cucurbit[7]uril	46%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

<u>Example 57</u>

Synthesis of cucurbit[n]urils in hydrochloric acid using tetraethylammonium chloride as an added template.

Glycoluril (142.1 mg), hydrochloric acid (36 % w/v, 0.7 mL) and tetraethylammonium chloride (28.2 mg) were placed in a reaction flask. Paraformaldehyde (60.0 mg) was added in one portion and the reaction mixture heated to 95°C for 2 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	0%
cucurbit[6]uril	10%
cucurbit[7]uril	70%
cucurbit[8]uril	18%
cucurbit[9]uril	<1%

cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 58

Synthesis of cucurbit[n]urils in hydrochloric acid using ammonium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and ammonium chloride (280 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	15%
cucurbit[6]uril	62%
cucurbit[7]uril	20%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 59

Synthesis of cucurbit[n]urils in hydrochloric acid using lithium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and lithium chloride (211 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	7%
cucurbit[6]uril	68%
cucurbit[7]uril	22%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 60

Synthesis of cucurbit[n]urils in hydrochloric acid using sodium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and sodium chloride (292 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	73%
cucurbit[7]uril	21%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 61

Synthesis of cucurbit[n]urils in hydrochloric acid using potassium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and potassium chloride (372 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	24%
cucurbit[6]uril	61%
cucurbit[7]uril	14%
cucurbit[8]uril	2%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 62

Synthesis of cucurbit[n]urils in hydrochloric acid using rubidium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and rubidium chloride (604 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	14%
cucurbit[6]uril	70%
cucurbit[7]uril	15%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 63

Synthesis of cucurbit[n]urils in hydrochloric acid using caesium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and caesium chloride (842 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	4%
cucurbit[6]uril	79%
cucurbit[7]uril	16%
cucurbit[8]uril	1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 64

Synthesis of cucurbit[n]urils in hydrobromic acid using ammonium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and ammonium bromide (490 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	8%
cucurbit[6]uril	66%
cucurbit[7]uril	23%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 65

Synthesis of cucurbit[n]urils in hydrobromic acid.

Glycoluril (1.49 g) and hydrobromic acid (48 % w/v, 6.9 mL) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	59%
cucurbit[7]uril	30%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 66

Synthesis of cucurbit[n]urils in hydrobromic acid using lithium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and lithium bromide (435 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	7%
cucurbit[6]uril	49%
cucurbit[7]uril	36%
cucurbit[8]uril	7%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 67

Synthesis of cucurbit[n]urils in hydrobromic acid using sodium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and sodium bromide (515 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	16%
cucurbit[6]uril	44%
cucurbit[7]uril	35%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

<u>Example 68</u>

Synthesis of cucurbit[n]urils in hydrobromic acid using sodium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and sodium bromide (5000 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	40%
cucurbit[6]uril	51%
cucurbit[7]uril	9%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

<u>Example 69</u>

Synthesis of cucurbit[n]urils in hydrobromic acid using potassium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and potassium bromide (595 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	36%
cucurbit[6]uril	44%
cucurbit[7]uril	18%
cucurbit[8]uril	2%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 70

Synthesis of cucurbit[n]urils in hydrobromic acid using rubidium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and rubidium bromide (827 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	25%
cucurbit[6]uril	43%
cucurbit[7]uril	24%
cucurbit[8]uril	8%
cucurbit[9]uril	<1%

cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 71

Synthesis of cucurbit[n]urils in hydrobromic acid using caesium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and caesium bromide (1070 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	15%
cucurbit[6]uril	59%
cucurbit[7]uril	23%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 72

Synthesis of cucurbit[n]urils in hydrochloric acid using ammonium chloride as an added template.

Glycoluril (1.49 g), hydrochloric acid (36 % w/v, 6.9 mL) and ammonium chloride (280 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 60°C for 60 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	11%
cucurbit[6]uril	60%
cucurbit[7]uril	21%
cucurbit[8]uril	8%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 73

Synthesis of cucurbit[n]urils in hydrobromic acid using rubidium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and rubidium bromide (827 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 60°C for 84 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	34%
cucurbit[6]uril	39%
cucurbit[7]uril	19%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 74

Synthesis of cucurbit[n]urils in hydrochloric acid using potassium chloride as an added template.

Glycoluril (250 g), hydrochloric acid (36 % w/v, 1200 mL) and potassium chloride (62 g) were placed in a reaction flask. Paraformaldehyde (110 g) was added in one portion and the reaction mixture heated to 95°C for 4 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	39%
cucurbit[6]uril	36%
cucurbit[7]uril	20%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 75

Synthesis of cucurbit[n]urils in hydrochloric acid using potassium chloride as an added template.

Glycoluril (8 g), hydrochloric acid (36 % w/v, 70 mL) and potassium chloride (2.1 g) were placed in a reaction flask. Paraformaldehyde (3.5 g) was added in one portion and the reaction mixture heated to 100°C for 3.5 hours. The reaction mixture was cooled and the products were collected by the removal of solvent on a rotary evaporator and analysed by NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	26%
cucurbit[6]uril	56%
cucurbit[7]uril	15%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 76

Synthesis of cucurbit[n]urils in hydrobromic acid using lithium bromide as an added template.

Glycoluril (1.49 g), hydrobromic acid (48 % w/v, 6.9 mL) and lithium bromide (4.3 g) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	13%
cucurbit[6]uril	63%
cucurbit[7]uril	22%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 77

Synthesis of cucurbit[n]urils in hydroiodic acid.

Glycoluril (1.49 g) and hydroiodic acid (57 % w/v, 6.9 mL) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to

100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield 2.2 g

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	72%
cucurbit[7]uril	22%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 78

Synthesis of cucurbit[n]urils in hydroiodic acid using lithium iodide as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and lithium iodide (665 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield 0.9 g

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	16%
cucurbit[6]uril	28%
cucurbit[7]uril	56%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 79

Synthesis of cucurbit[n]urils in hydroiodic acid using sodium iodide as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and sodium iodide (745 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	19%
cucurbit[6]uril	55%
cucurbit[7]uril	17%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 80

Synthesis of cucurbit[n]urils in hydroiodic acid using potassium iodide as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and potassium iodide (825 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	67%
cucurbit[6]uril	22%

cucurbit[7]uril	10%
cucurbit[8]uril	1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 81

Synthesis of cucurbit[n]urils in hydroiodic acid using rubidium iodide as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and rubidium iodide (1060 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	34%
cucurbit[6]uril	18%
cucurbit[7]uril	48%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 82

Synthesis of cucurbit[n]urils in hydroiodic acid using caesium iodide as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and caesium iodide (1300 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	8%
cucurbit[6]uril	36%
cucurbit[7]uril	53%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 83

Synthesis of cucurbit[n]urils in hydroiodic acid using red phosphorous as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and red phosphorous (1 g) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	70%
cucurbit[7]uril	23%
cucurbit[8]uril	4%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 84

Synthesis of cucurbit[n]urils in hydroiodic acid using lithium iodide and red phosphorous as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and lithium iodide and red phosphorous (665 mg and 650 mg respectively) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	23%
cucurbit[6]uril	6%
cucurbit[7]uril	65%
cucurbit[8]uril	6%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 85

Synthesis of cucurbit[n]urils in hydroiodic acid using sodium iodide and red phosphorous as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and sodium iodide and red phosphorous (745 mg and 650 mg respectively) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vaccum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	57%
cucurbit[6]uril	9%
cucurbit[7]uril	29%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 86

Synthesis of cucurbit[n]urils in hydroiodic acid using potassium iodide and red phosphorous as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and potassium iodide and red phosphorous (825 mg and 650 mg respectively) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	75%
cucurbit[6]uril	11%
cucurbit[7]uril	10%
cucurbit[8]uril	3%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 87

Synthesis of cucurbit[n]urils in hydroiodic acid using rubidium iodide and red phosphorous as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and rubidium iodide and red phosphorous (1060 mg and 650 mg respectively) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	58%
cucurbit[6]uril	20%
cucurbit[7]uril	20%
cucurbit[8]uril	2%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 88

Synthesis of cucurbit[n]urils in hydroiodic acid using caesium iodide and red phosphorous as an added template.

Glycoluril (1.49 g), hydroiodic acid (57 % w/v, 6.9 mL) and caesium iodide and red phosphorous (1300 mg and 650 mg respectively) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 2 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtation.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	21%
cucurbit[6]uril	28%
cucurbit[7]uril	46%
cucurbit[8]uril	5%
cucurbit[9]uril	<1%

cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 89

Synthesis of cucurbit[n]urils in sulfuric acid using potassium sulfate as an added template.

Glycoluril (1.49 g), sulfuric acid (9 M, 6.9 mL) and potassium sulfate (436 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	15%
cucurbit[6]uril	66%
cucurbit[7]uril	18%
cucurbit[8]uril	1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 90

Synthesis of cucurbit[n]urils in sulfuric acid using potassium sulfate as an added template.

Glycoluril (1.49 g), sulfuric acid (9 M, 6.9 mL) and potassium sulfate (871 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	11%
cucurbit[6]uril	75%
cucurbit[7]uril	15%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 91

Synthesis of cucurbit[n]urils in sulfuric acid using potassium sulfate as an added template.

Glycoluril (1.49 g), sulfuric acid (9 M, 6.9 mL) and potassium sulfate (1307 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	33%
cucurbit[6]uril	49%
cucurbit[7]uril	16%
cucurbit[8]uril	2%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 92

Synthesis of cucurbit[n]urils in sulfuric acid using potassium sulfate as an added template.

Glycoluril (1.49 g), sulfuric acid (9 M, 6.9 mL) and potassium sulfate (4350 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the

reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	23%
cucurbit[6]uril	64%
cucurbit[7]uril	13%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 93

Synthesis of cucurbit[n]urils in sulfuric acid using lithium sulfate as an added template.

Glycoluril (1.49 g), sulfuric acid (9 M, 6.9 mL) and lithium sulfate (275 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	4%
cucurbit[6]uril	71%
cucurbit[7]uril	24%
cucurbit[8]uril	1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 94

Synthesis of cucurbit[n]urils in sulfuric acid using lithium sulfate as an added template.

Glycoluril (1.49 g), sulfuric acid (9 M, 6.9 mL) and lithium sulfate (2750 mg) were placed in a reaction flask. Formalin (40% w/v) (1.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	25%
cucurbit[6]uril	51%
cucurbit[7]uril	23%
cucurbit[8]uril	1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 95

Synthesis of cucurbit[n]urils in hydrochloric acid using lithium chloride as an added template.

Glycoluril (5 g), hydrochloric acid (36 % w/v, 20 mL) and lithium chloride (746 mg) were placed in a reaction flask. Paraformaldehyde (2.2 g) was added in one portion and the reaction mixture heated to 100°C for 4 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	22%
cucurbit[6]uril	37%

cucurbit[7]uril	29%
cucurbit[8]uril	12%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 96

Synthesis of cucurbit[n]urils in p-toluenesulfonic acid using lithium p-toluenesulfonate as an added template.

Glycoluril (400 mg), p-toluenesulfonic acid (~95 %, 3.5 g) and lithium p-toluenesulfonate (157 mg) were placed in a reaction flask. Formalin (40% w/v) (0.5 mL) was added in one portion and the reaction mixture heated to 100°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and collected by vacuum filtration.

Yield 240 mg

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	18%
cucurbit[6]uril	45%
cucurbit[7]uril	26%
cucurbit[8]uril	9%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 97

Synthesis of cucurbit[n]urils with hydrochloric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), hydrochloric acid (36 % w/v, 1 drop) and trifluoroacetic acid (1 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 3 hours. The reaction mixture was cooled and the

products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	46%
cucurbit[6]uril	54%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 98

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 2 drops) and trifluoroacetic acid (1 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 4 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 99

Synthesis of cucurbit[n]urils with hydrochloric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), hydrochloric acid (36 % w/v, 5 drops) and trifluoroacetic acid (1 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 5 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 100

Synthesis of cucurbit[n]urils with hydrochloric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg) and trifluoroacetic acid (1 mL) were placed in a reaction flask. Dry hydrochloric acid gas was then bubbled into the solution for 15 minutes. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 20.5 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Exmaple 101

Synthesis of cucurbit[n]urils with hydrochloric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg) trifluoroacetic acid (2 mL) were placed in a reaction flask. Dry hydrochloric acid gas was then bubbled into the solution for 15 minutes. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 25 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 102

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 23 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	37%
cucurbit[7]uril	39%
cucurbit[8]uril	24%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 103

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 2 drops) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 23 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and he collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%

cucurbit[11]uril <1%

Example 104

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 23 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	48%
cucurbit[7]uril	32%
cucurbit[8]uril	20%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 105

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 3 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril <1%

cucurbit[6]uril	57%
cucurbit[7]uril	28%
cucurbit[8]uril	15%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 106

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (fuming, 3 drops) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 25.5 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	47%
cucurbit[7]uril	34%
cucurbit[8]uril	20%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 107

Synthesis of cucurbit[n]urils with sulfuric acid using methanesulfonic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop) and methanesulfonic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 26 hours. The reaction mixture was cooled and the

products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	5%
cucurbit[6]uril	62%
cucurbit[7]uril	33%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 108

Synthesis of cucurbit[n]urils with sulfuric acid using methanesulfonic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops) and methanesulfonic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 26 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	7%
cucurbit[6]uril	61%
cucurbit[7]uril	32%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 109

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (fuming, 3 drops) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 26 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	47%
cucurbit[7]uril	35%
cucurbit[8]uril	17%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 110

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoroacetic acid as a solvent.

Glycoluril (144 mg), sulfuric acid (fuming, 3 drops) and trifluoroacetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 26 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	47%

cucurbit[7]uril	32%
cucurbit[8]uril	21%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 111

Synthesis of cucurbit[n]urils with sulfuric acid using 1,1,1-trifluoroethanol as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop) and 1,1,1-trifluoroethanol (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 25 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	17%
cucurbit[6]uril	72%
cucurbit[7]uril	11%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 112

Synthesis of cucurbit[n]urils with sulfuric acid using 1,1,1-trifluoroethanol as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops) and 1,1,1-trifluoroethanol (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 25 hours. The reaction mixture was cooled and the

products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	89%
cucurbit[6]uril	11%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

<u>Example 113</u>

Synthesis of cucurbit[n]urils with sulfuric acid using 1,1,1-trifluoroethanol as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop) and 1,1,1-trifluoroethanol (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 170 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 114

Synthesis of cucurbit[n]urils with sulfuric acid using 1,1,1-trifluoroethanol as a solvent.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops) and 1,1,1-trifluoroethanol (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 170 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	100%
cucurbit[7]uril	<1%
cucurbit[8]uril	<1%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 115

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoro acetic acid as a solvent and o-carborane as a template.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop), o-carborane (18 mg) and trifluoro acetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 25.5 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	57%
cucurbit[7]uril	32%
cucurbit[8]uril	11%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 116

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoro acetic acid as a solvent and o-carborane as a template.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops), o-carborane (18 mg) and trifluoro acetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 25.5 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR
Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	50%
cucurbit[7]uril	32%
cucurbit[8]uril	17%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 117

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoro acetic acid as a solvent and o-carborane as a template.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop), o-carborane (18 mg) and trifluoro acetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 20 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	51%
cucurbit[7]uril	39%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 118

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoro acetic acid as a solvent and o-carborane as a template.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops), o-carborane (18 mg) and trifluoro acetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 20 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	<1%
cucurbit[6]uril	47%
cucurbit[7]uril	38%
cucurbit[8]uril	15%
cucurbit[9]uril	<1%

cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 119

Synthesis of cucurbit[n]urils with sulfuric acid using trifluoro acetic acid as a solvent and o-carborane as a template.

Glycoluril (710 mg), sulfuric acid (98 % w/v, 7.5 mL), o-carborane (18 mg) and trifluoro acetic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 24.5 hours. The reaction mixture was cooled and the products were precipitated by addition of methanol and the collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	3%
cucurbit[6]uril	53%
cucurbit[7]uril	33%
cucurbit[8]uril	11%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 120

Synthesis of cucurbit[n]urils with sulfuric acid using methanesulfonic acid as a solvent and o-carborane as a template.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 1 drop), o-carborane (18 mg) and methanesulfonic acid (7.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 22.5 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

cucurbit[5]uril	7%
cucurbit[6]uril	53%
cucurbit[7]uril	30%
cucurbit[8]uril	10%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

Example 121

Synthesis of cucurbit[n]urils with sulfuric acid using methanesulfonic acid as a solvent and o-carborane as a template.

Glycoluril (144 mg), sulfuric acid (98 % w/v, 5 drops), o-carborane (18 mg) and methanesulfonic acid (1.5 mL) were placed in a reaction flask. Paraformaldehyde (63 mg) was added in one portion and the reaction mixture heated to 90°C for 22.5 hours. The reaction mixture was cooled and the products were pecipitated by addition of ethanol and collected using a centrifuge.The collected solid was then dried at 80°C overnight and analysed by ^{13}C NMR.

Yield >98 % by NMR

Approximate Yields by ^{13}C NMR (mass % of recovered product)

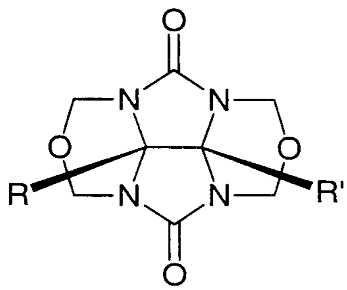
cucurbit[5]uril	6%
cucurbit[6]uril	56%
cucurbit[7]uril	30%
cucurbit[8]uril	8%
cucurbit[9]uril	<1%
cucurbit[10]uril	<1%
cucurbit[11]uril	<1%

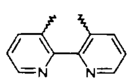
Examples 122

Preparation of Substituted Cucurbiturils

Substituted glycolurils of the following formulae were used in this synthesis:

Examples of mixed cucurbit[s,u]urils



'tetracyclic diether' R=R'=CH_3, dimethyl; R=R'=C_6H_5, diphenyl; R=R'=  , dihydrophenathroline.

(1) A mixture of the dimethyl tetracyclic diether (107mg) and caesium chloride (71mg) in concentrated hydrochloric acid (0.5ml) was heated at 100°c for 1hr 40mins. to give a >85% yield of the decamethylcucurbit[5]uril and <1% of the other sizes.

(2) A mixture of the dimethyl tetracyclic diether (97 mg) and glycoluril (54mg) in concentrated hydrochloric acid (0.5ml) was shaken at room temperature for 1hr then heated at 100°C for 1hr 40 mins., at which time reaction was complete. The yield was determined by ^{13}C NMR to be >95% for a mixture of the methyl substituted cucurbit[s,u]urils, where s,u equals1,4; 2,3; 3,2; 4,1; 1,5; 2,4; 3,3; 4,2; 5,1; 1,6; 2,5; 3,4; 4,3; 5,2; 6,1; and s represents the unit carrying the substitution. The composition of s to u was determined by ES-MS.

(3) A mixture of the dimethyl tetracyclic diether (119mg), glycoluril (66mg) and caesium chloride (78mg) in concentrated hydrochloric acid (0.5ml) was shaken at room temperature for 1 hr then heated at 100°C until the reaction was complete at 1hr 20mins.

The yield by ^{13}C NMR was near quantitative. The composition of s to u was observed to be different but not accurately determined.

(4) The diphenyl tetracyclic diether (1.9gm), gylcoluril (0.71gm) and para toluene sulphonic acid (10.4gm) were combined and heated to 120°C for 3hr. While still hot the mixture was poured into methanol (150ml) and precipitate collected by filtration. The solid material collected was dissolved in a minimum volume of hot formic acid and this solution was poured into hot water and the precipitate collected to give 1.32gm of the phenyl substituted cucurbit[s,u]urils, where s,u equals 1,4; 2,4; 2,4; 3,3 and s represents the unit carrying the substitution.

(6) To a suspension of the dihydrophenathroline glycoluril (530mg) in aqueous 40% formaldehyde was added 8M hydrochloric acid (1.8ml) and the mixture stirred at room temperature for 5hr. Then glycoluril (253mg) was added and the mixture heated at 100°C for 3hr. ^{13}C NMR of the mixture indicated a 20-30% formation of the dihydrophenanthroline substituted cucurbit[s,u]urils.

Variations of these methods could conceivably be applied to any substituted glycoluril where the side chain is stable to the reaction conditions.

Template function

The controlling factors for achieving the synthesis of a variety of cucurbiturils of differing unit sizes are postulated to be primarily derived from a templating effect. For example, an anion is apparently held in position by a metal cation or the ammonium ion. The metal cations coordinate to the carbonyls of the forming cucurbituril intermediates (such as **F**, **G1** and **G2**) or in the case of the ammonium cation is held through hydrogen bonding to the carbonyls of these intermediates. The larger iodide anion and its tight pairing with the lithium cation favours cucurbit[7]uril but for the more diffuse ion pairs of sodium, potassium, or rubidium, iodide does not control the size by templating around the anion but rather templating is predominantly controlled by the cation although this effect diminishes as the anion decreases in size. There has been found a common trend where the equilibrium shifts by varying combinations of anion and cations. The proton from the acid not only serves as a catalyst but also acts as a cation capable of hydrogen bonding to the

carbonyls of the forming cucurbit[n]uril and also controlling the placement of anions. The degree of the competing influence between these protons and any added cations affects the equilibrium and hence the product distribution. Cucurbit[n]urils where n>7 appears to be controlled by a templating around a cation/anion cluster rather than a single ion pair. Electrospray mass spectroscopy of larger cucurbiturils supports this showing multi charged cationic complexes.

Further influences upon the equilibrium and hence the product out come is the precipitation of product complexes. For example increasing the concentration by 10 times of a cation such as lithium in sulphuric acid changes the relative proportion of cucurbit[5]uril from 5% to 25% as a consequence of the precipitation of the cucurbit[5]uril lithium complexes.

In addition to equilibrium shifts caused by changes to the cation concentration the equilibrium is also affected by the formation of the cucurbit[6]uril iodine complex which occurs under the reaction conditions where hydriodic acid is used and hydriodic acid decomposes to form iodine. The addition of red phosphorus eliminates this effect by the *in situ* reduction of the iodine generated.

In addition, we have found that a wide range of other inorganic and organic compounds can be used as templates. These affect the equilibrium through a variety of subtle effects including ion-dipole, diople-diople and hydrogen bonding, hydrophobic and weak Van der Waals interactions. In essence, any material or compound stable to the reaction conditions could act as a potential template.

Industrial applicability

The potential uses for cucurbit[n]urils are large with academic, industrial, analytical and pharmaceutical applications. As a class these molecules can be favourable compared to the cyclodextrins because both molecular systems posses a hydrophobic cavity with polar end caps. Cyclodextrins have been used in a wide range of applications including slow release drugs, odour entrapment agents in plastic films, and enzimimics for synthesis. It is believed that cucurbit[n]urils will be of use in similar areas where benefit can be taken of the ability of the cucurbit[n]urils to take up molecules or compounds into there central cavity. Such potential uses may include:

Environmental (water and soil)

Remediation, by the binding of polluting products and their removal:

- Preventative, eg, by binding of potential pollutants before wastes are released to the environment;

- Uses in biodegradable polymers.

Domestic and Public

- Incorporation into polymers as odourisers, releasing fragrances slowly over time;

- Or incorporated into polymers to trap unpleasant odours or toxic vapours

- Encaptulation of bleaching and whitening agents.

Food

- Flavour enhancers;

- Flavour optimisers, hence hiding unpleasant flavours:

- Polyphenol removal to reduce discolouration of juices.

Pharmaceutical

- Slow release drugs, limiting side effects and reducing the frequency of doses;

- Increasing drug stability in vivo or on the shelf;

- Detoxification, for example, decreasing stomach irritations, or the treatment of chemical allergens by encaptulation.

Agricultural/horticultural

- Slow release of herbicides and pesticides;

- Stabilisation of agricultural chemicals against light and heat.

Manufacturing

- Enzyme/catalyst mimics;

- Regioselective control over reaction products;

- Manipulation of paint and polymer products;

- Chromatographic columns for chemical purification;

- Analytical tools and devices;

- Printing and photography.

Miscellaneous

- Volatility reduction, for storage, safety, or use;

- Uses for insensitive munitions manufacture;

- Forensic science.

Cucurbit[n]urils are thermally more robust than cyclodextrins and are stable to strong acid solutions unlike cyclodextrins.

The present inventors have also found that cucurbit[6]uril and cucurbit[7]uril can both bind dioxane aqueous solutions. This dioxane binding property can form the basis of processes for the removal of dioxane. According to a further aspect of the present invention, the

present invention provides a process for removing dioxane from a fluid comprising contacting the fluid with cucurbit[6]uril and/or cucurbit[7]uril.

The physical removal of dioxane could take place using one of the following techniques:

- Cucurbit[6 or 7]uril bound to a non-reactive solid support (silica or alumina) where the dioxane would bind to the cucurbit[6 or 7]uril and then be removed from solution by simple filtration to collect the solid support.
- A solution of cucurbit[6 or 7]uril placed in dialysis tubing which would allow the passage of dioxane into the solution where it would be bound by the cucurbit[6 or 7]uril.
- Incorporation of the cucurbit[6 or 7]uril into a solid clay support and use filtration techniques to remove bound dioxane.
- Incorporation into a polymer film. In this case the dioxane would be entrapped by the cucurbit[6 or 7]uril inside the polymer film. When the capacity of the film has been reached it is simply removed from contact with the product stream.
- In all cases the material itself could be regenerated for repeated use.

If the dioxane is contained in the solid, for example in dioxane/contaminated soil, the process of this aspect of the invention may comprise the further step of washing the soil with a fluid to thereby cause the dioxane to go into the fluid and subsequently treating the fluid in accordance with this aspect of the invention.

Cucurbit[5]uril has shown uptake of carbon monoxide. Accordingly, the invention further provides a method for removing carbon monoxide from a liquid or vapour containing carbon monoxide by contacting the liquid or vapour with cucurbit[5]uril.

The present invention provides a method for producing a range of cucurbit[n]urils and cucurbit[s,u]urils. The synthesis method results in the production of a number of cucurbit[n]urils and cucurbit[s,u]urils that have never before been produced or isolated. Separation is possible via chromatography and/or selective precipitation. The product cucurbit[n]urils and cucurbit[s,u]urils are stable to vigorous reaction conditions over a wide range of pH values. They are soluble in aqueous acid or aqueous salt solutions. The

method gives cucurbiturils in much larger yields than previously possible. The use of templating compounds allows a degree of control over the relative amounts of the different cucurbit[n]urils being produced.

Those skilled in the art will appreciate that the invention described herein may be susceptible to variation and modifications other than those specifically described. It is to be understood that the present invention encompasses all such variations and modifications that fall within its spirit and scope.

The claims defining the invention are as follows:

1. A method for producing cucurbit[n]urils, where n is from 4 to 12, comprising mixing substituted and/or unsubstituted glycoluril with an acid and a compound that can form methylene bridges between glycoluril units, and heating the mixture to a temperature of from 20° to 120° to thereby form cucurbit[n]urils.

2. A method as claimed in claim 1 wherein n is from 4 to 10.

3. A method as claimed in claim 1 or claim 2 further comprising adding a templating compound to the mixture.

4. A method as claimed in claim 3 wherein said templating compound is selected from ammonium chloride, lithium chloride, sodium chloride, potassium chloride, rubidium chloride, caesium chloride, ammonium chloride, lithium bromide, sodium bromide, potassium bromide, rubidium bromide, caesium bromide, lithium iodide, sodium iodide, potassium iodide, rubidium iodide, caesium iodide, potassium sulfate, lithium sulfate, tetrabutylammonium chloride, tetraethylammonium chloride, 0-carborane, thioacetamide, N-(1-napthyl) ethylenediamine, 2,2'-biquinoyl, p-bromoanaline, taurine, blue tetrazolium, 2-amino-3-methyl benzoic acid, indol-3-aldeyde, cystine, p-acetamidonitine, p-aminophenol, acetamide, 4-acetamidoanitine, p-aminophenol, acetamide, 4-aminoacetophenone, 4-dimethylaminobenzaldehyde, 2-aminobenzimadazol, bis-(4,4'-bipyridyl)-α, α'-p-xylene, red phosphorus, and lithium p-toluenesulfonate.

5. A method as claimed in claim 3 wherein the templating compound is a salt.

6. A method as claimed in claim 5 wherein the anion of the salt corresponds to the anion of the acid in the mixture.

7. A method as claimed in any one of claims 3 to 6 wherein two or more templating compounds are added to the mixture.

8. A method as claimed in any one of the preceding claims wherein the acid comprises a strong mineral acid or a strong organic acid.

9. A method as claimed in any one of the preceeding claims wherein the acid is selected from sulfuric acid, hydrochloric acid, hydrobromic acid, hydroiodic acid, deuterated sulfuric acid, phosphoric acid, p-toluenesulfonic acid, and methane sulfonic acid.

10. A method as claimed in any one of the preceding claims further comprising adding a solvent to the reaction mixture.

11. A method as claimed in claim 10 wherein the solvent is selected from trifluoroacetic acid, methanesulfonic acid and 1,1,1-trifluoroethanol.

12. A method as claimed in any one the preceding claims wherein the compound that can form methylene bridges between glycoluril units comprises formaldehyde, paraformaldehyd, trioxane or one or more precursors for formaldehyde.

13. A method as claimed in any one of the preceding claims wherein the mixture is heated to a temperature of from 20°C to 110°C.

14. A method as claimed in claim 13 wherein the mixture is heated to a temperature of from 60° to 110°C.

15. A method as claimed in claim 13 wherein the mixture is heated to a temperature of from 80° to 110°C.

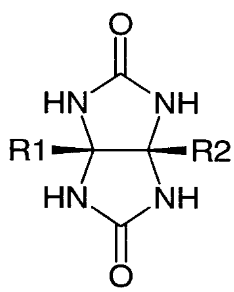
16. A method as claimed in any one of the preceding claims wherein the mixture is heated for between 1 hour and 24 hours.

17. Cucurbit[n]uril, where n = 4, 5, 7, 8, 9, 10, 11 or 12.

18. Substituted cucurbiturils of the formula cucurbit[s,u]uril, wherein s = number of substituted glycoluril units and s + u = 4 to 12.

19. A method for producing substituted cucurbiturils of the formula cucurbit[s,u]urils, where s = number of substituted glycoluril units, u = number of unsubstituted glycoluril units and s + u = 4 to 12 comprising mixing substituted glycoluril and unsubstituted glycoluril with an acid and a compound that can form methylene bridges between glycoluril units and heating the mixutre to a temperature of from 20° to 120°to thereby form cucurbit[s,u]urils.

20. A method as claimed in claim 19 wherein the substituted glycoluril has a formula



wherein R_1 and R_2 are the same or different and selected from an optionally substituted straight chain, branched or cyclic, saturated or unsaturated hydrocarbon radical or R_1 and R_2 form a cyclic hydrocarbon radical.

21. A method as claimed in claim 20 wherein the hydrocarbon radical for substituents R_1 and R_2 is the same or different and selected from alkyl, alkenyl, alkynyl, aryl and heterocyclyl radicals.

22. A method as claimed in any one of claims 19 to 21 wherein s + u = 4 to 10.

23. A method as claimed in any one of claims 19 to 22 further comprising adding a templating compound to the mixture.

24. A method as claimed in claim 23 wherein said templating compound is selected from ammonium chloride, lithium chloride, sodium chloride, potassium chloride, rubidium chloride, caesium chloride, ammonium chloride, lithium bromide, sodium bromide, potassium bromide, rubidium bromide, caesium bromide, lithium iodide, sodium iodide, potassium iodide, rubidium iodide, caesium iodide, potassium sulfate, lithium sulfate, tetrabutylammonium chloride, tetraethylammonium chloride, 0-carborane, thioacetamide, N-(1-napthyl) ethylenediamine, 2,2'-biquinoyl, p-bromoanaline, taurine, blue tetrazolium, 2-amino-3-methyl benzoic acid, indol-3-aldeyde, cystine, p-acetamidonitine, p-aminophenol, acetamide, 4-acetamidoanitine, p-aminophenol, acetamide, 4-aminoacetophenone, 4-dimethylaminobenzaldehyde, 2-aminobenzimadazol, bis-(4,4'-bipyridyl)-α, α'-p-xylene, red phosphorus, and lithium p-toluenesulfonate.

25. A method as claimed in claim 23 where said templating compound is a salt.

26. A method as claimed in claim 25 wherein the anion of the salt corresponds to the anion of the acid in the mixture.

27. A method as claimed in any one of claims 23 to 26 wherein two or more templating compounds are added to the mixture.

28. A method as claimed in any one of claims 19 to 27 wherein the acid comprises a strong mineral acid or a strong organic acid.

29. A method as claimed in any one of claims 19 to 28 wherein the acid is selected from sulfuric acid, hydrochloric acid, hydrobromic acid, hydroiodic acid, deuterated sulfuric acid, phosphoric acid, p-toluenesulfonic acid, and methane sulfonic acid.

30. A method as claimed in any one of claims 19 to 29 further comprising adding a solvent to the mixture.

31. A method as claimed in claim 30 wherein the solvent is selected from trifluoroacetic acid, methane sulfonic acid and 1,1,1-trifluoroethanol.

32. A method as claimed in any one of claims 19 to 31 wherein the compound that can form methylene bridges between glycoluril units comprises formaldehyde, paraformaldehyde, trioxane or one or more precursors for formaldehyde.

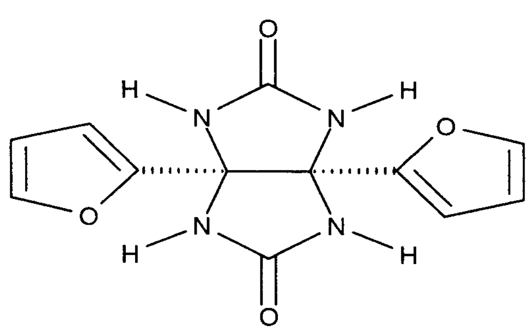
33. A method as claimed in any one of claims 19 to 32 wherein the mixture is heated to a temperature of from 20° to 110°C.

34. A method as claimed in claim 33 wherein the mixture is heated to a temperature of from 60° to 110°C.

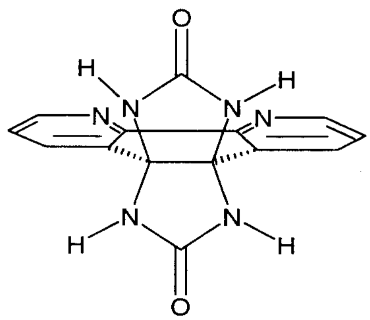
35. A method as claimed in claim 33 wherein the mixture is heated to a temperature of from 80° to 110°C.

36. A method as claimed in any one of claims 19 to 35 wherein the mixture is heated for between 1 hour and 24 hours.

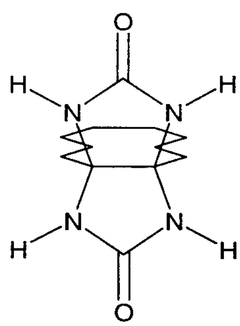
37. A substituted glycoluril of the formula:



38. A substituted glycoluril of the formula:



39. A substituted glycoluril of the formula:



40. A method for separating a mixture of cucurbit[n]urils, where n = 4 to 12, by mixing the mixture of cucurbit[n]urils, dissolves, separating solids in which at least one of the cucurbit[n]urils, but not all of the cucurbit[n]urils, dissolves, and separating solids from the solution.

41. A method as claimed in claim 40 further comprising recovering at least one cucurbit[n]uril from the solids.

42. A method as claimed in claim 40 further comprising recovering at least one cucurbit[n]uril from solution.

43. A method as claimed in claim 42 further comprising passing the solution into contact with an ion exchange resin to thereby absorb dissolved cucurbit[n]urils onto the resin and subsequently eluting said cucurbit[n]urils from the resin.

44. A method for separating a mixture of cucurbit[n]urils, where n = 4 to 10, by dissolving the mixture of cucurbit[n]urils and subjecting the thus-formed solution of cucurbit[n]urils to chromatographic separation.

45. A method for separating a mixture of cucurbit[s,u]urils where s = number of substituted glycoluril units, u = number of unsubstituted glycoluril units and s + u = 4 to 12 comprising dissolving the mixture of cucurbit[s,u]urils and subjecting the thus-formed mixture of cucurbit[s,u]urils to chromatographic separation.

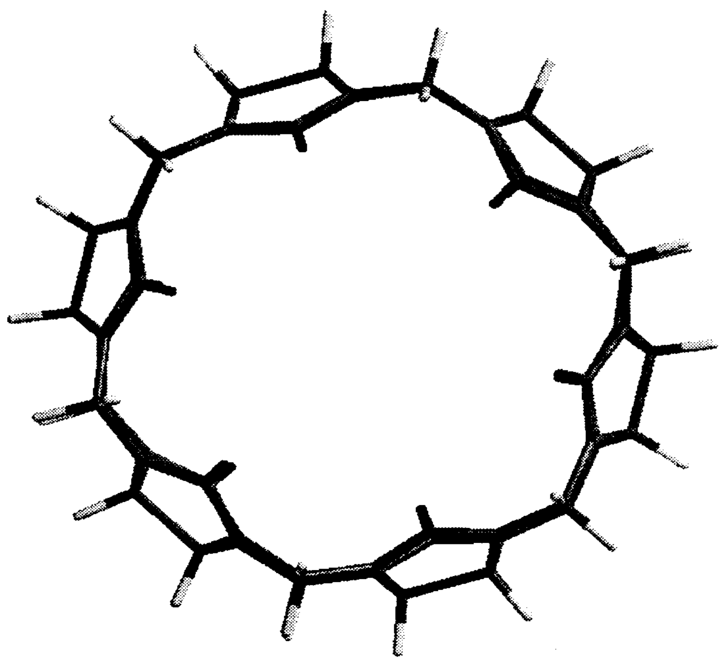
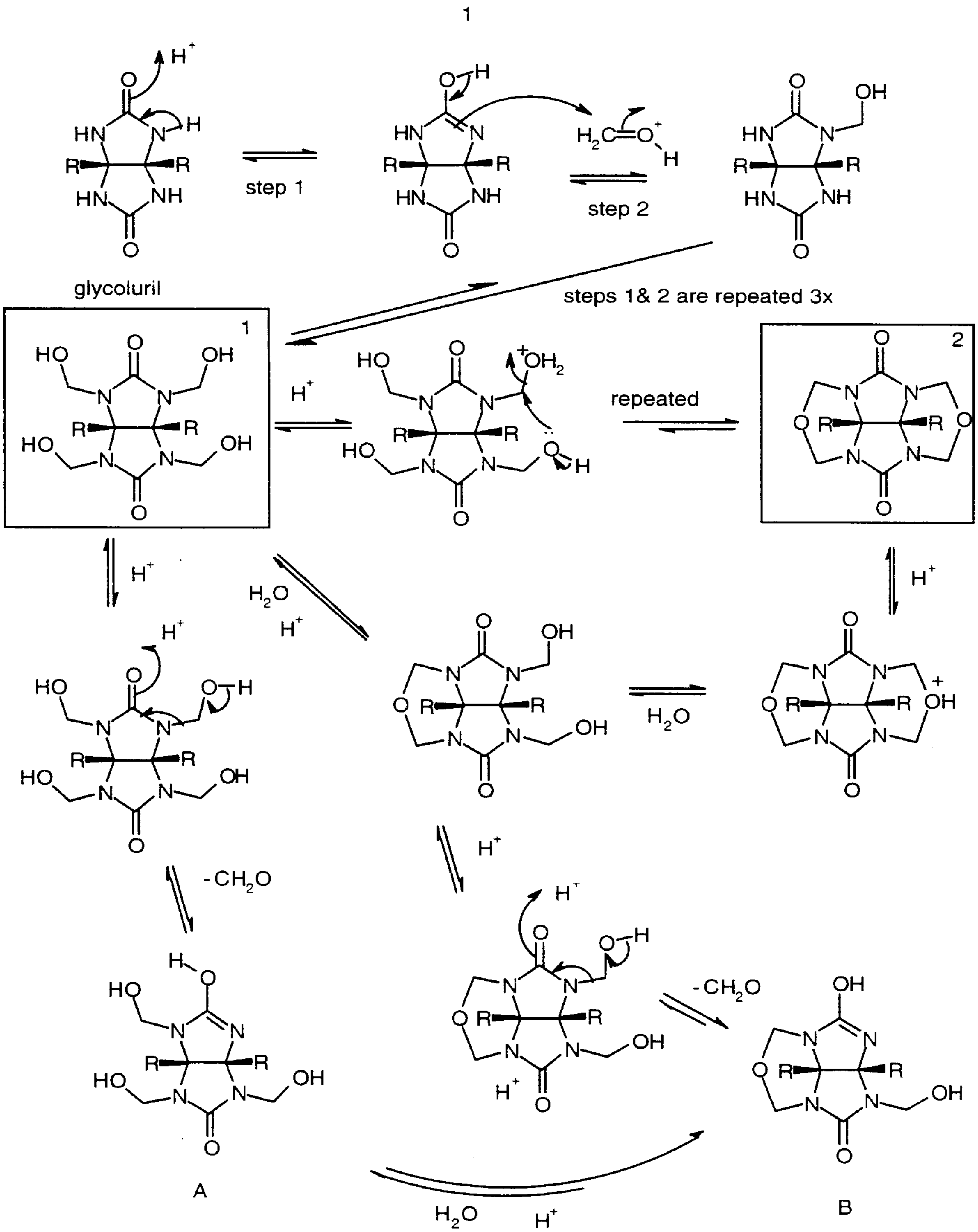


FIGURE 1



1. F.G.M. Niele and R.J.M. Nolte *J. Am. Chem. Soc.* **1988**, 110, 172
2. J.W.H. Smeets, R. P. Sijbesma, L. van Dalen, A.L. Spek, W.J.J. Smeets, and R.J.M. Nolte,*J. Org. Chem.* **1989**.54,3710.

FIGURE 1a

3/9

2

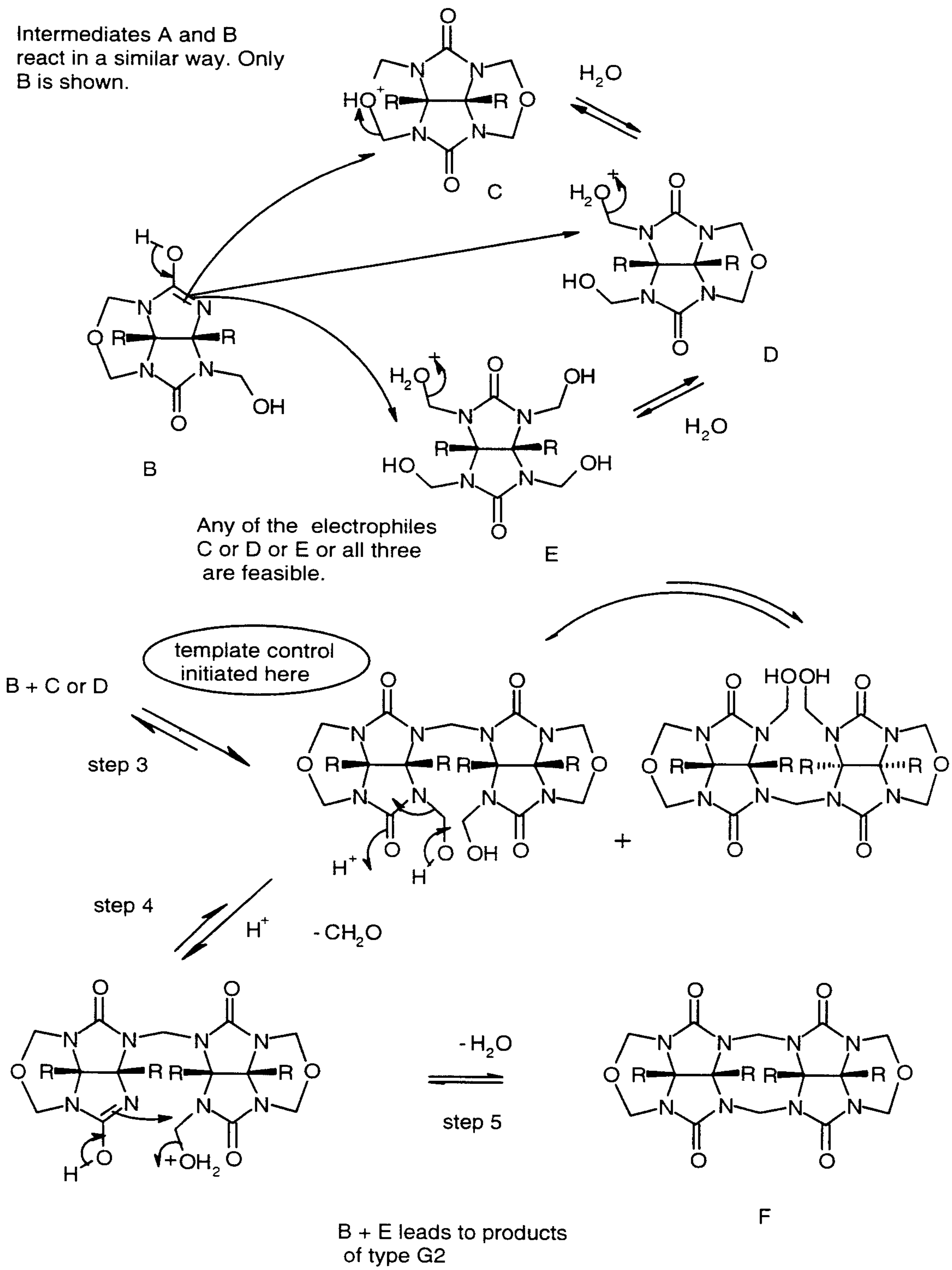
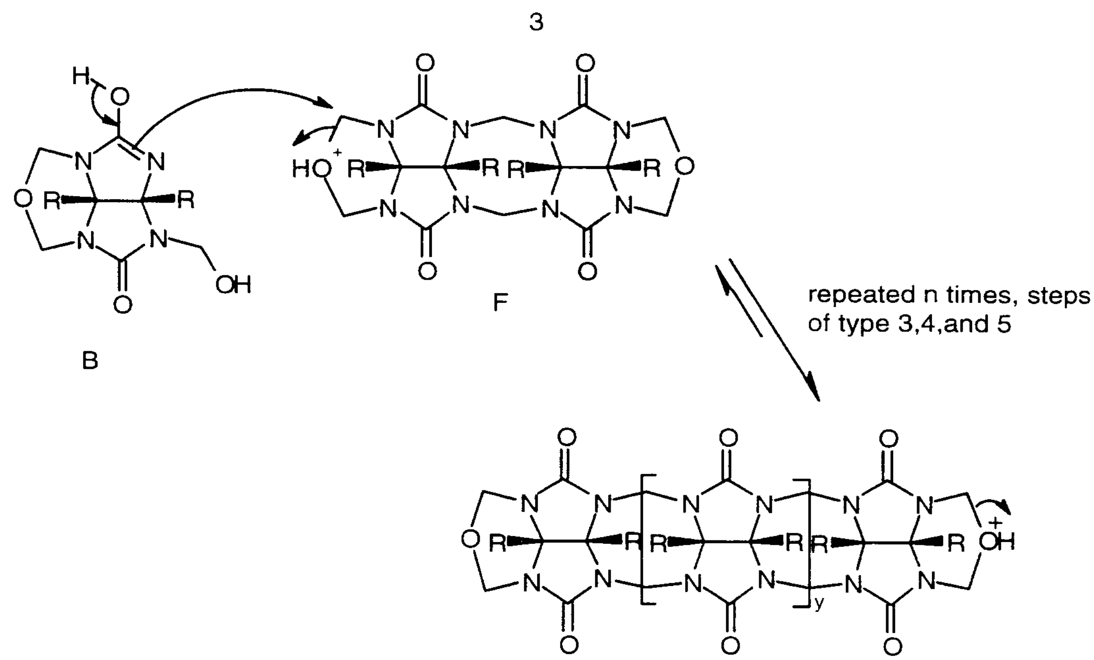
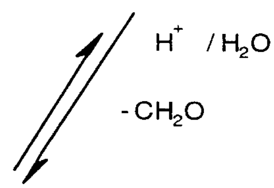


FIGURE 1b

3





B can be as shown or any nucleophile related to B, eg G1 and G2 as shown below as derived from a dimer or any polymeric unit of similar structure.

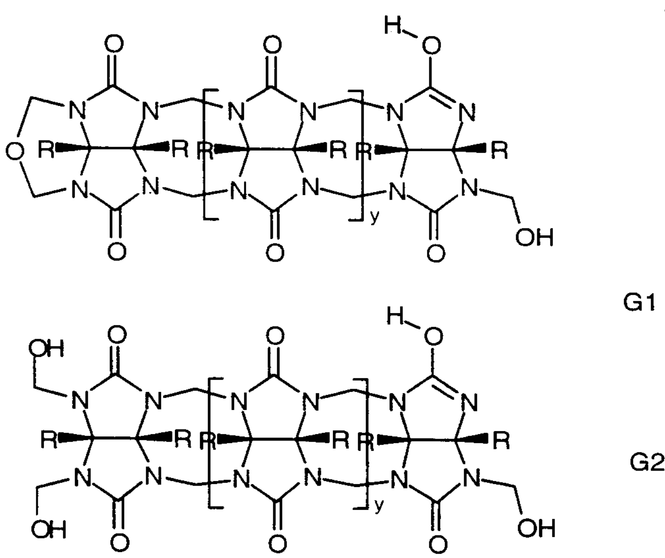


FIGURE 1c

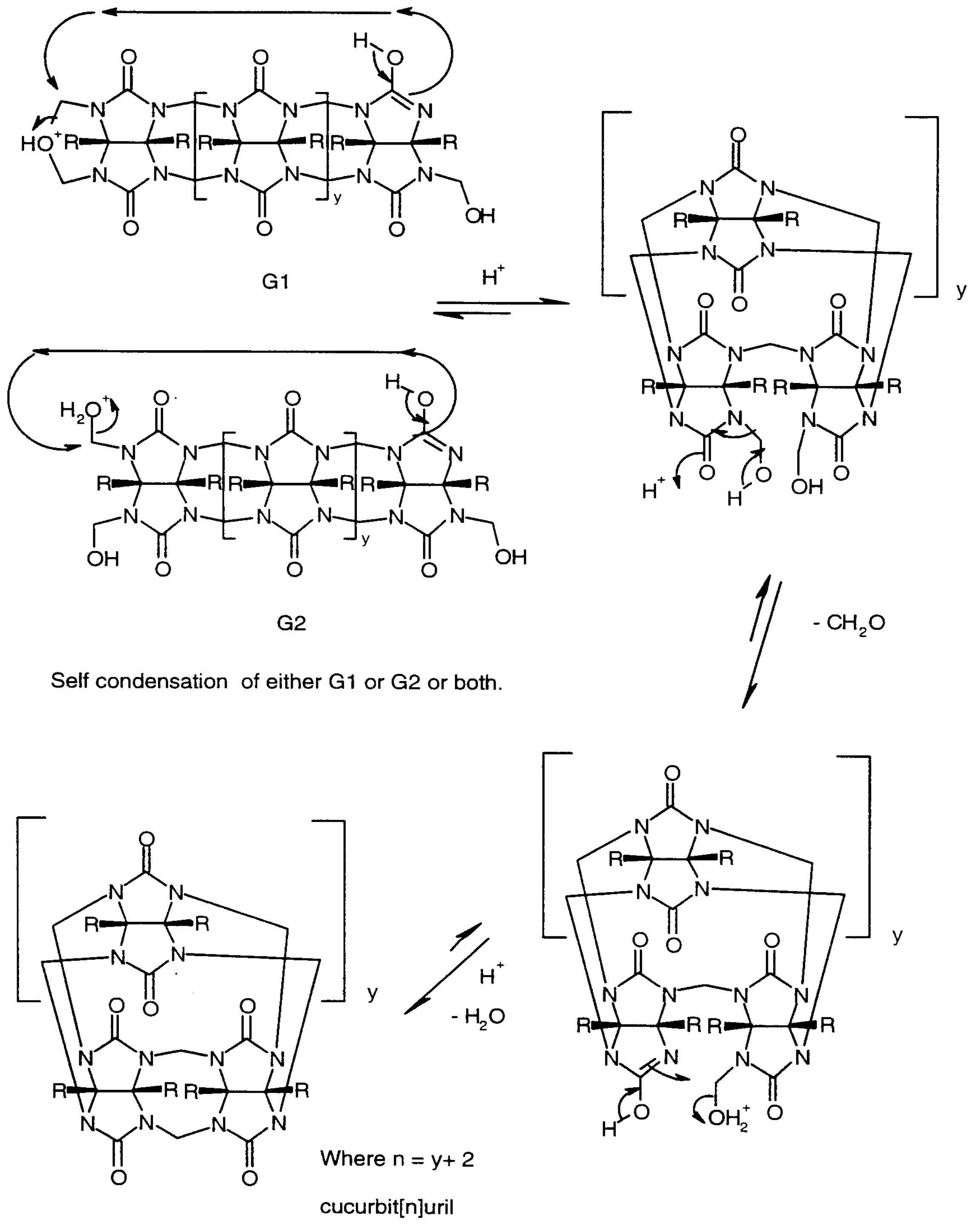
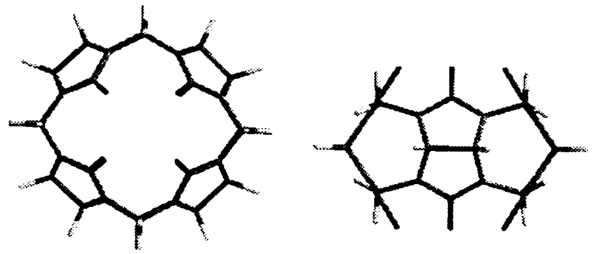
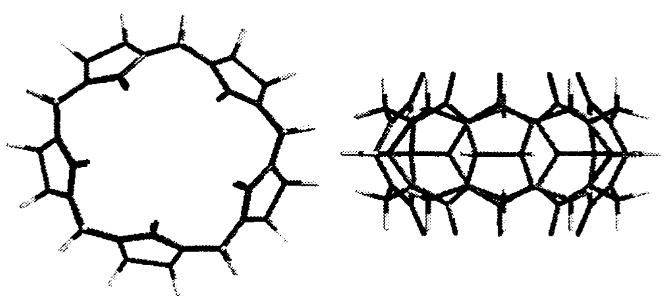

G1
H+
G2
- CH2O
Self condensation of either G1 or G2 or both.
H+
- H2O
Where n = y+ 2
cucurbit[n]uril

FIGURE 1d



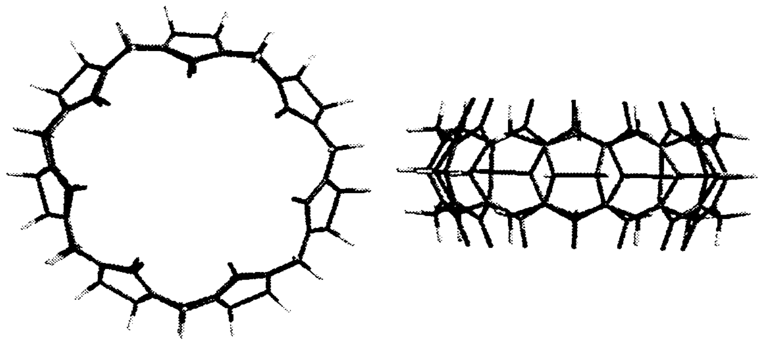
FORMULA 8

FIGURE 2



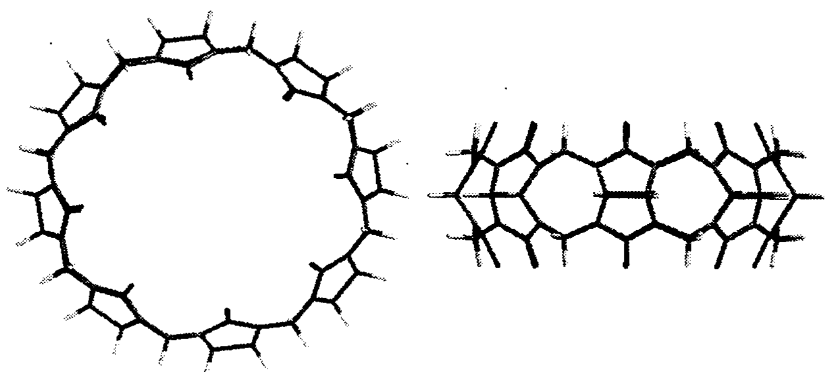
FORMULA 9

FIGURE 3



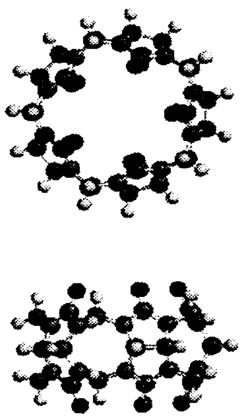
FORMULA 10

FIGURE 4

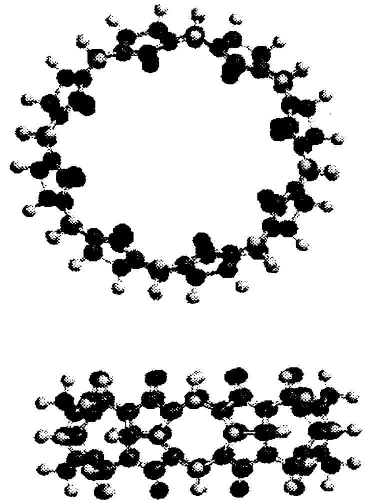


FORMULA 11

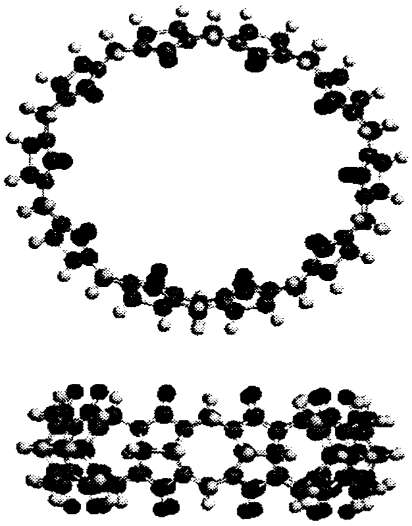
FIGURE 5



FORMULA 12



FORMULA 13



FORMULA 14

FIGURE 5a

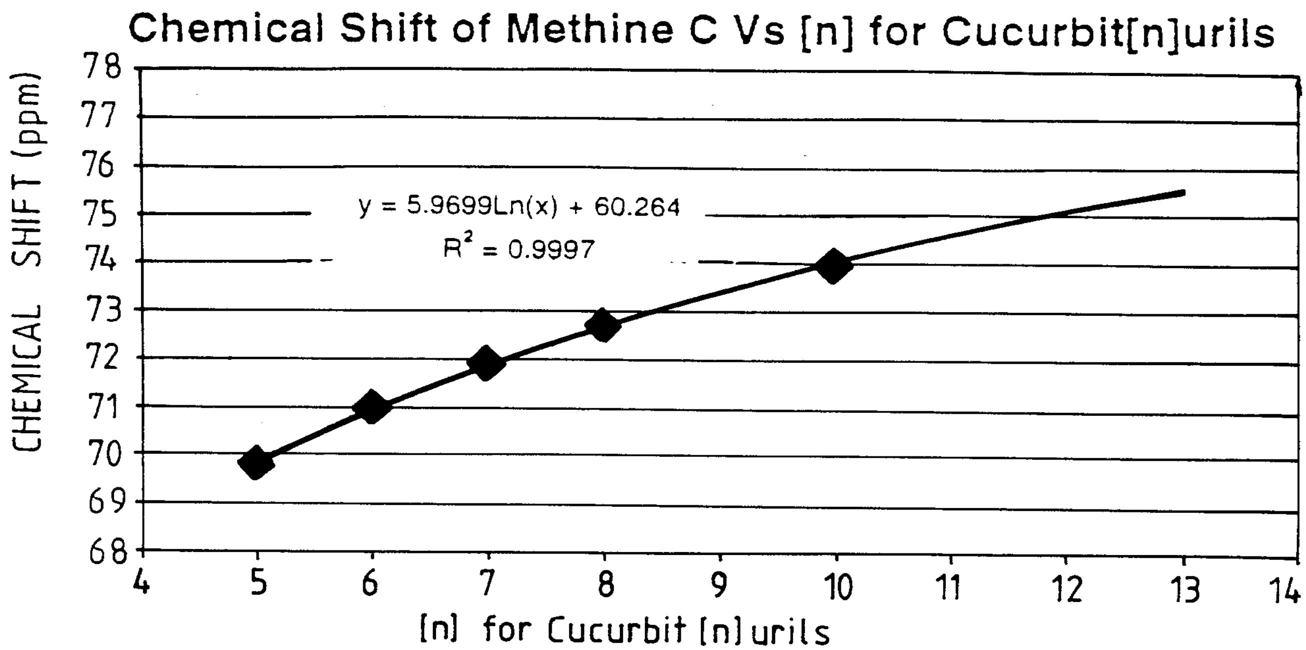

Chemical Shift of Methine C Vs [n] for Cucurbit[n]urils
CHEMICAL SHIFT (ppm)
78
77
76
75
74
73
72
71
70
69
68
y = 5.9699Ln(x) + 60.264
R² = 0.9997
4
5
6
7
8
9
10
11
12
13
14
[n] for Cucurbit [n] urils

FIG. 6.

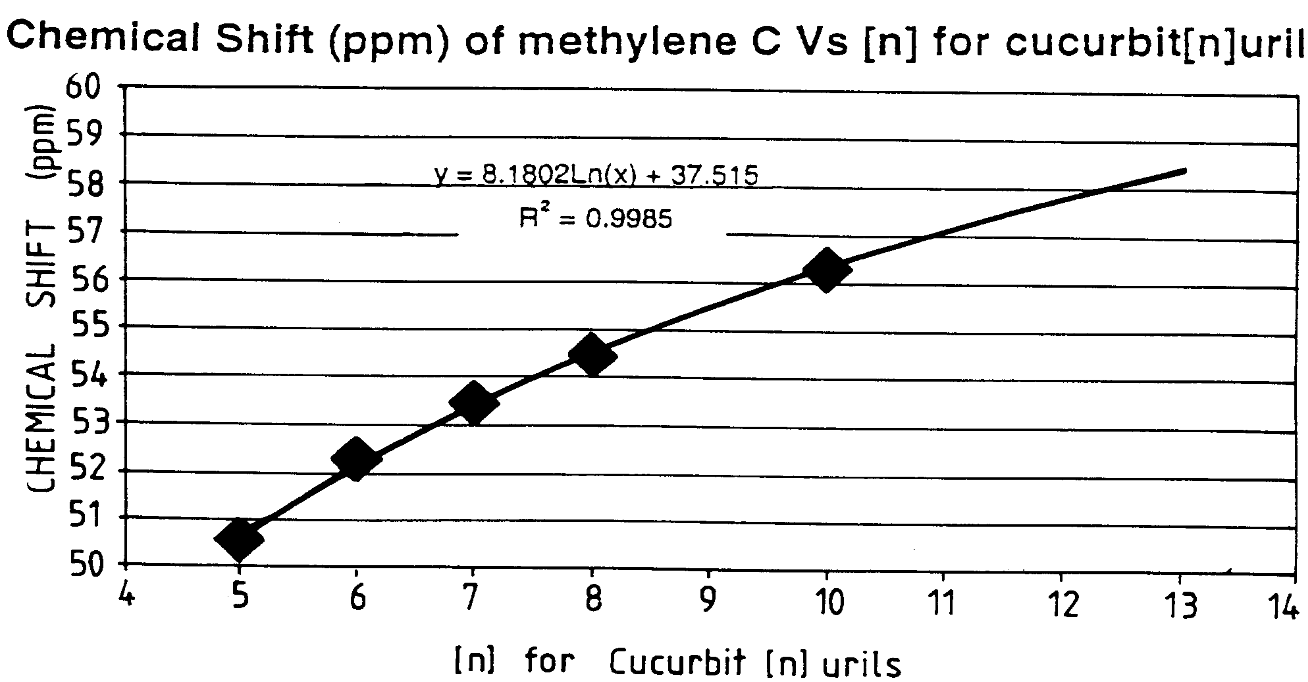

Chemical Shift (ppm) of methylene C Vs [n] for cucurbit[n]uril
CHEMICAL SHIFT (ppm)
60
59
58
57
56
55
54
53
52
51
50
y = 8.1802Ln(x) + 37.515
R² = 0.9985
4
5
6
7
8
9
10
11
12
13
14
[n] for Cucurbit [n] urils

FIG. 7.

INTERNATIONAL SEARCH REPORT	International application No. PCT/AU00/00412

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. ^{7}: C07D 487/22, 487/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Chemical Abstracts: substructure, as well as glycoluril

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	Angew. Chem. Int. Ed. Engl. 1992, 31, No. 11, pp 1475-1477, A. Flinn et al.; "Decamethylcucurbit[5]uril" See whole article, particularly last 2 sentences of last paragraph on page 1475, Fig. 1, and Experimental Procedure	1, 2, 8-10, 12-22, 28-30, 32-36
X, Y	DE 4001139 A1 (Deutsches Textilforschungszentrum) 25 October 1990 See Example 1	1, 2, 8-10, 12-16, 18-22, 28-30, 32-36
X	Chemical Abstracts, Abstract no. 129:183422, 1998, J.A.A.W. Elemans et al.; "Bipyridine functionalized molecular clips. Self-assembly of their ruthenium complexes in water" See abstract, formula I and Chemical Abstracts Registry Number 211382-70-6	38

[X] Further documents are listed in the continuation of Box C [ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 June 2000	07 JUL 2000
Name and mailing address of the ISA/AU	Authorised officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**G. D. HEARDER** Telephone No : (02) 6283 2553

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU00/00412

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	J. Am. Chem. Soc. 2000, 122, pp 540-541, 8 January 2000, J. Kim et al.; "New Cucurbituril Homologues: Syntheses, Isolation, Characterization, and X-ray Crystal Structures of Cucurbit[*n*]uril (n = 5, 7, and 8)" See whole article	1-36, 40-45
A	DE 19603377 A1 (Deutsches Textilforschungszentrum) 7 August 1997 See example	1-45
A	Inorganica Chimica Acta, 193 (1992) pp 93-97, H.J. Buschmann et al.; "Cucurbituril as a ligand for the complexation of cations in aqueous solutions" See whole article, particularly p 93	1-45